302.00 Human Research Protections Program Policy

1.1 Scope

This Institution's Human Research Protection Program (HRPP) is a comprehensive system to ensure the protection of the rights and welfare of subjects in human research. The Human Research Protection Program is based on all individuals in this Institution along with key individuals and committees fulfilling their roles and responsibilities described in this plan. Throughout this document "Institution" refers to Pennington Biomedical Research Center.

1.2 Purpose

This Institution is committed to protecting the rights, safety, welfare, and wellbeing of subjects in human research. The purpose of this plan is to describe this Institution's plan to comply with ethical and legal requirements for the conduct and oversight of human research.

1.3 Definitions

1.3.1 Agent

An individual who is an employee is considered an **agent** of this Institution for purposes of engagement in human research when that individual is in any official capacity as an employee of this Institution.

An individual who is not an employee is considered an agent of this Institution for purposes of engagement in human research when that individual has been **specifically authorized** to conduct human research on behalf of this Institution.

1.3.2 Principal Investigator, Co-Investigator or Investigator

Principal Investigator ("PI"), Co-Investigator or Investigator is an individual who conducts research or under whose immediate direction research is conducted; or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team. NIH PHS 398

Investigator means an individual who actually conducts a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team. FDA 21 CFR 50.3.25(d)

For the purposes of this Institution Principal Investigators must be a member of the regular faculty, adjunct faculty, or a member of the faculty of one of the institutions affiliated with the Pennington Biomedical Research Center. Professionals in training (graduate students, post-doctoral researchers, interns, and residents) are permitted to be Principal Investigators as long as they have at least one regular Pennington faculty member, with the appropriate background and training to conduct the research, serve as a Sub-Investigator and, if applicable, permitted by their home institution policies.

1.3.3 Engaged in Human Research

This Institution is engaged in human research when its employees or agents are interacting or intervening with human subjects for the purpose of conducting research. This Institution follows the Office of Human Research Protections (OHRP) guidance on “Engagement of Institutions in Research” to apply this definition.

The Institution defines all research according to the DHHS definition, unless the clinical trial is subject to FDA oversight.

1.3.4 Human Research

Any activity that either:

- Is “research” as defined by DHHS and involves “human subjects” as defined by DHHS (“DHHS Human Research”); or DHHS 45 CFR 46.102
- Is “research” as defined by FDA and involves “human subjects” as defined by FDA (“FDA Human Research”). FDA 21 CFR 56.102.22(c); 21 CFR 50.3.25 (c)

1.3.5 Research as Defined by DHHS

Research as defined by DHHS is a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

The institution defines all research according the DHHS definition, unless the clinical trial is subject to FDA oversight. 45 CFR 46.102(d)

Research activities that are specifically deemed not to be research:

1. Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

2. Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

3. Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

4. Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions.

Generalizable Knowledge means information from which one may infer a general conclusion: knowledge brought into general use or that can be applied to a wider or different range of circumstances. For example, publication and presentation are typical methods used to disseminate research findings, thereby contributing to generalizable knowledge. However, not all information that is published or presented represents generalizable knowledge. Generalizable knowledge is also interpreted to include data intended for general use, regardless of its eventual distribution or acceptance.

1.3.6 Research as Defined by FDA

Clinical investigation or research as defined by FDA means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit. The term does not include experiments that are subject to the provisions of part 58 of this

chapter, regarding nonclinical studies. The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous.

[21 CFR 50.3(c) and 21 CFR 56.102(c)]

1.3.7 Human Subject as Defined by DHHS

A **human subject** as defined by DHHS is a living individual about whom an investigator (whether professional or student) conducting research (1) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens, or (2) obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens. For the purpose of this definition:

1.3.8 Definitions of Human Subject as Defined by DHHS

- **Intervention** means physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.

- **Interaction** means communication or interpersonal contact between investigator and subject.

- **Private Information** means information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record).

- **Identifiable private Information** means private information that is individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information).

- **An identifiable biospecimen** is a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen.

When following DHHS regulations policies, a reexamination of the meaning of "private identifiable information" and "identifiable biospecimen" shall take place at least every four years, or when updated in the Federal Register per CRF46.102 (e)(7)

DHHS 45 CFR §46.102(b), 102(e)(7)

1.3.9 Human Subject as Defined by FDA

A **human subject** as defined by the FDA is an individual who is or becomes a subject in research, either as a recipient of the test article or as a control. A subject may be either a healthy human or a patient. A human subject includes an individual on whose specimen (identified or unidentified) a medical device is used. When medical device research involves in vitro diagnostics and unidentified tissue specimens, the FDA defines the unidentified tissue specimens as human subjects. FDA 21 CFR 56.23(e)

1.3.10 Clinical Trial Definitions as Defined by NIH & OHRP

A **clinical trial** is a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of those interventions on health-related biomedical or behavioral outcomes.

- The term *"prospectively assigned"* refers to a pre-defined process (e.g., randomization) specified in an approved protocol that stipulates the assignment of research subjects (individually or in clusters) to one or more arms (e.g., intervention, placebo, or other control) of a clinical trial.

- An *"intervention"* is defined as a manipulation of the subject or subject's environment for the purpose of modifying one or more health-related biomedical or behavioral processes and/or endpoints. Examples include: drugs/small molecules/compounds; biologics; devices; procedures (e.g., surgical techniques); delivery systems (e.g., telemedicine, face-to-face interviews); strategies to change health-related behavior (e.g., diet, cognitive therapy, exercise, development of new habits); treatment strategies; prevention strategies; and, diagnostic strategies.

- A *"health-related biomedical or behavioral outcome"* is defined as the pre-specified goal(s) or condition(s) that reflect the effect of one or more interventions on human subjects' biomedical or behavioral status or quality of life. Examples include: positive or negative changes to physiological or biological parameters (e.g., improvement of lung capacity, gene expression); positive or negative changes to psychological or neurodevelopmental parameters (e.g., mood management intervention for smokers; reading comprehension and /or information retention); positive or negative changes to disease processes; positive or negative changes to health-related behaviors; and, positive or negative changes to quality of life.

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1.4 Mission

The mission of this Institution's human research protection program plan is to protect the rights, safety, welfare and wellbeing of subjects involved in human research overseen by this Institution. Concern for the interests of the subject should prevail over the interests of science and society. All human subject research is subject to the human research protection program plans policies and procedures.

The HRPP includes mechanisms to:

- Establish a formal process to monitor, evaluate and continually improve the protection of human research participants;
- Exercise oversight of research protection;
- Educate IRB members, IRB support staff, investigators and research staff about their ethical responsibility to protect research participants;
- When appropriate, intervene in research and respond directly to concerns of research participants;
- Educate research participants and the community.
- Ensure sufficient coordination among the components of the HRPP and dedicate resources sufficient to carry out the above tasks.

1.4.1 Ethical Requirements

In the oversight of all human research, this Institution (including its investigators, research staff, students involved with the conduct of human research, the Institution's Institutional Review Board (IRB), IRB members and chair, IRB staff, the Institutional official, and employees) follows the ethical principles outlined in the April 18, 1979 report of The National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research titled "Ethical Principles and Guidelines for the Protection of Human Subjects of Research," also known as "The Belmont Report", which includes:

- Respect for Persons
- Beneficence
- Justice

1.4.2 Legal and Regulatory Requirements

The HRPP is responsible for ensuring compliance by the institution and its investigators with applicable federal, state, and local laws and regulations (including 45 CFR 46 and 21 CFR 50 and 56) and institutional policies governing human subject research under its auspices.

All human research must undergo review by the Institution's IRB. Activities that do not meet the definition of human research (e.g., most classroom activities, quality improvement activities, program evaluation, and surveillance activities that do not meet the definition of human research) do not require review and approval by the Institution IRB and do not need to be submitted to the Institution IRB unless there is a question regarding whether the activity is human research.

When this Institution is engaged in DHHS human research that is conducted, funded, or otherwise subject to regulations by a federal department or agency who is a signatory of the Common Rule, the Institution commits to apply the regulations of that agency relevant to the protection of human subjects.

When this Institution is engaged in FDA human research, it commits to apply the FDA regulations relevant to the protection of human subjects.

Any questions about whether an activity meets the regulatory definitions of human research should be referred to the IRB Office who will provide a determination.

1.4.3 Other Requirements

- This Institution commits to apply its ethical standards to all human research regardless of funding.
- For clinical trials, this Institution commits to apply the "International Council on Harmonization – Good Clinical Practice E6." International Research studies must adhere to recognized ethics codes such as: The Common Rule and the Declaration of Helsinki. (World Medical Association Declaration of Helsinki, A1,2)
- This Institution prohibits payments to professionals, meaning individuals and not entities, in exchange for referrals of potential subjects ("finder's fees") and payments designed to accelerate recruitment that were tied to the rate or timing of enrollment ("bonus payments.") FDA Guidance "Payment to Research Subjects"
- When Human Research is conducted or funded by the Department of Defense (DOD), this Institution commits to apply the Department of Defense (DOD) Directive 3216.02, which includes the requirement to apply 45 CFR §46

Subparts B, C, and D[1]. This Institution will comply with the terms of the DFARS clause or comparable language used in the agreement with the Department of Defense (DOD) component supporting the research involving human subjects. See HRPP Policy 15.0 for Research Funded by the Department of Defense.

- When Human Research is conducted or funded by the Department of Education (ED), this Institution commits to applying 34 CFR §97 Subpart D (equivalent to 45 CFR §46 Subpart D), 34 CFR §98.3, 34 CFR §98.4, 34 CFR §356.3, and 34 CFR §99. See HRPP Policy 16.0 for Research Funded by the Department of Education

1.4.3.1 Research in Other Countries

- All policies and procedures that are applied to Human Research conducted domestically are applied to Human Research conducted in other countries.
    - For research conducted in other countries the PI must ensure the following:
        - Knowledge of local law and cultural context is sufficient to inform decisions about how the research is conducted.
        - qualifications of the researchers and research staff for conducting research in that country.
        - The consent process is appropriate to the population, coordination and communication with local IRBs when appropriate.
    - When research is conducted outside the United States, the IRB will:
        - Ensure activities are consistent with the ethical principles in the HRPP policies and that the participants are afforded protections that are at least equivalent to the ethical standards outlined in the Belmont Report.
        - Ensure appropriate expertise and knowledge of the country(ies) either through IRB members or consultants.
        - Ensure knowledge of local laws.

[1] Quick applicability table for DHHS Subparts:

	DHHS	DOD	ED
Subpart B	X	X	
Subpart C	X	X	
Subpart D	X	X	X

- Ensure knowledge of cultural context.
- Confirm the qualifications of the researchers and research staff for conducting research in that country.
- Ensure Initial review, continuing review, and review of modifications to previously approved research.
- Ensure post-approval monitoring.
- Handle of complaints, noncompliance, and unanticipated problems involving risk to subjects or others.
- Ensure procedures for Consent process and document and other language issues.
- Ensure coordination and communication with local IRBs when appropriate. Some examples of ways of ensuring knowledge of the laws of other countries might include:
    - Rely upon an IRB or EC in the country.
    - Using a consultant with expertise in the country.
    - Partnering with an organization such as a nonprofit that regularly works in the country.

1.4.4 Scope of Human Research Protection Program

The categories of human research overseen by the IRB include:

- Research conducted or funded by the Department of Defense (DOD). For additional requirements of research conducted by the Department of Defense, see Guidance G-003: Additional Requirements Conducted by the Department of Defense
- Federally funded research
- Research involving fetuses.
- FDA-regulated research.
- Research involving drugs that require an IND.
- Research involving devices that require an IDE issued by FDA.
- Research involving pregnant women as subjects.
- Research involving non-viable neonates.
- Research involving neonates of uncertain viability.
- Research involving children as subjects.

- International research
- Research conducted or funded by the Department of Education (ED)
- Research involving children, pregnant women, fetuses, or neonates that is not otherwise approvable without approvable of an agency secretary or director.
- Investigator held IND or IDE.
- Research involving devices that require an abbreviated IDE.
- Investigator held abbreviated IDE.

The categories of human research not overseen include:

- Research conducted or funded by the Veteran Administration (VA)
- Research conducted or funded by the Department of Justice (DOJ)
- Research conducted or funded by the Department of Energy (DOE)
- Research conducted, funded, or subject to oversight by the Environmental Protection Agency (EPA)
- Research involving *in vitro* fertilization.
- Research that plans to or is likely to involve prisoners as subjects.
- Research involving a waiver of consent for planned emergency research.
- Emergency use of a test article in a life threatening situation.
- Activities involving humanitarian use devices.
- Research using the short form of consent documentation.
- Classified Research

1.4.5 Human Research Protection Program Policies and Procedures

Pennington Biomedical Research Center Policies and procedures are made available for all Pennington Biomedical investigators and research staff at the following web site: http://pbrc.edu/HRPP. Pennington Biomedical uses the HRPP website to communicate policies and procedures, guidance to investigators and staff, required forms, and contact information for the HRPP office.

1.5 Human Research Protection Program Components

The components comprising the HRPP and their responsibilities, ethical obligations, and authorities for carrying out the mission of the program are described below.

1.5.1 Institutional Official

The Executive Director of Pennington Biomedical Research Center is designated as the Institutional Official. The Institutional Official (IO) is the individual who is legally authorized to act for the institution and, on behalf of the institution, obligates the institution to the Terms of the Federal-wide Assurance.

The general administrative obligations of the Institutional Official are including but not limited to:

- Designating one or more Institutional Review Boards (IRBs) that will review research covered by the institution's FWA;
- Providing sufficient resources, meeting space, and staff to support the IRB's review and record keeping duties;
- Ensuring that adequate resources, including funds, meeting space, and personnel are provided to support the operation of the HRPP;
- Providing training and educational opportunities for the IRB and investigators;
- "Setting the tone" by promoting an institutional culture of respect and conscience, so that the ethical conduct of human subjects research is supported at the highest levels of the organization;
- Ensuring effective institution-wide communication and guidance on human subjects research;
- Ensuring that investigators fulfill their responsibilities;
- Encouraging that all staff engaged in the conduct or oversight of human subject research participate in education activities;
- Serving as a knowledgeable point of contact for OHRP and other federal agencies, or delegating the responsibility to another appropriate individual;
- Granting the IRB authority to act independently to bind the entire organization, including but not limited to the Institutional Official with regards to human subjects protections.

Regulations: Federalwide Assurance (FWA) for the Protection of Human Subjects

The Institutional Official may delegate the performance of certain oversight and operational duties (listed below) to one or more individuals. Any delegation of duty must be in writing. Upon designation of a new Institutional Official, all delegation letters must be reviewed and renewed by the new Institutional Official if the new Institutional Official chooses to maintain delegation.

- Appointing IRB members. Suspending or terminating the IRB membership of any individual for whom it has been determined that he/she is not fulfilling membership responsibilities and or obligations;
- Appointing the IRB chair or co-chairs. Suspending or terminating the appointment of any chair or co-chair who is not fulfilling his/her responsibilities and or obligations;
- Performing periodic evaluation of the performance of the IRB chairs and co-chairs and administrative staff;

- Managing and administering funds. Ensuring that adequate personnel, space and other resources are allocated to the HRPP;
- Reviewing and signing memoranda of understanding and cooperative agreements between the institution and other organizations, including those that establish reliance on IRBs of record for collaborative research (e.g., IRB Authorization Agreements, Individual Investigator Agreements);
- Being the point of contact for correspondence addressing human subjects research with the OHRP, FDA and other agencies as applicable, including reports to federal agencies;
- Ensuring that IRB members and investigators are knowledgeable to conduct research in accordance with ethical standards and all applicable regulations;
- Developing and implementing an educational plan for IRB members, staff and investigators;
- Ensuring that IRB members and investigators are knowledgeable to conduct research in accordance with ethical standards and all applicable regulations;
- Performing periodic evaluation of the performance of the IRB members and administrative staff;
- Recruiting qualified members to include expert, non-scientific and unaffiliated representation on the IRB;
- Reviewing and approving Standard Operating Procedures (SOPs) for the IRB and HRPP;
- Overseeing daily operations of the IRB and HRPP in accordance with the SOPs.
- Assessing this plan periodically to determine whether it is providing the desired results and recommending amendments as needed.
- Establishing policies and procedures designed to increase the likelihood that human research will be conducted in accordance with ethical and legal requirements.

The following responsibilities of the Institutional Official should not be delegated to a designee:

- Signatory authority for the FWA;
- Ensuring that the IRB functions independently and that its chair or chairs and members have direct access to the Institutional Official for appeal if they experience undue influence or if they have concerns about the function of the IRB;
- Ensuring that adequate resources, including funds, space, and personnel are provided to support the operation of the HRPP.
- The Institutional Official or the designee cannot approve research that has been disapproved (or not yet approved) by the IRB.
- HHS CFR 46.112 and the terms of the institution’s FWA

1.5.2 All members of the Institution

All individuals within the Institution have the responsibility to:

- Be aware of the definition of human research (see section 1.3.4).
- Consult the IRB when there is uncertainty about whether an activity is human research.
- Ensure all human subjects research is approved by the IRB.
- Report allegations of undue influence regarding the oversight of the Human Research Protection Program or concerns about the Human Research Protection Program to the Institutional Official.
- Report allegations or finding of non-compliance with the requirements of the Human Research Protection Program to the IRB.
- Research involving human participants must not commence until the research has received all approvals required by the organization.

1.5.3 IRB

The IRB designated by the Institutional Official is to be the IRB relied upon by the Human Research Protection Program and the scope of review of this IRB is listed in the IRB roster available from the IRB Office.

Competing business interests can influence the review process when individuals responsible for business development serve on the IRB are involved in the day to day operations of the IRB. Therefore, no individual responsible for raising funds or garnering support for research should serve as an IRB member or be involved in the day to day operations of the IRB.

Individuals who are responsible for business development are prohibited from:

- Serving as members or ex-officio members on the IRB.
- IRB members are prohibited from owning equity in the organization, if appropriate.

The IRB functions independently of, but in coordination with, other institutional departments. The IRB, however, makes its independent determination whether to approve or disapprove a protocol based upon whether or not human subjects are adequately protected. The IRB has review jurisdiction over all research involving human subjects, conducted, supported or otherwise subject to regulation by any federal department or agency that has adopted the human subject regulations.

Consistent with federal regulations, no one within the institution may approve human subjects research that has not been approved by the IRB. However, research

approved by the IRB may be subject to further institutional review, approval or disapproval.

Consistent with the federal regulations, the IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities constituting non-exempt human subjects research under the regulations. Furthermore, the IRB shall conduct continuing review of research as appropriate to the degree of risk (in federally-funded research, no less than annually). The IRB shall also suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects.

IRB approval notwithstanding, research involving human participants must not commence until all institutional requirements are met and institutional approval to proceed has been obtained.

This Institution may rely upon IRBs of another Institution provided one of the following is true:

- The IRBs are part of an AAHRPP accredited Institution.
- This Institution’s investigator is a collaborator on Human Research that is primarily conducted at another Institution and the investigator’s role does not include interaction or intervention with subjects.
- The Institution is engaged in the Human Research solely because it is receiving federal funds. (Employees and agents of the institution do not interact or intervene with subjects, gather or possess private identifiable information about subjects, nor obtain the consent of subjects.)

Reliance on an external IRB requires an Institutional Agreement for IRB review (IAIR) and a local review for compliance with local policies of the Institution. These requirements must be formalized and in place before the Institution will accept any human research proposals from the other institution or rely on the review of the other institution.

The IRBs relied upon by this Institution have the authority to:

- Approve, require modifications to secure approval, and disapprove all human research overseen and conducted by the Institution. All human research must be approved by the IRB designated by the Institutional Official. Officials of this Institution may not approve human research that has not been approved by one of the Institution’s IRBs.

- Suspend or terminate approval of human research not being conducted in accordance with a IRBs' requirements or that has been associated with unexpected serious harm to subjects.
- Observe, or have a third party observe, the consent process and the conduct of the human research.
- Determine whether an activity is human research as described in HRPP Policy 3.0. 45 CFR 46.102(d)
- Evaluate financial interests of investigators and research staff and have the final authority to decide whether the financial interest and management plan, if any, allow the human research to be approved. PBRC Policy 401.00

IRB member and IRB staff have the responsibility to follow Human Research Protection Program policies and procedures that apply to IRB members and staff.

1.5.4 Investigators and Research Staff

Investigators and research staff have the responsibility to:

- Follow the Human Research Protection Program policies and procedures that apply to IRB members and staff.
- Comply with all determinations and additional requirements of the IRB, the IRB chair, and the Institutional Official.
- Oversee the review and conduct of Human Research in their department or laboratory.
- Forward complaints and allegations regarding the Human Research Protection Program to the Institutional Official or designee.
- Ensure that each Human Research study conducted in their department or laboratory has adequate resources.

1.5.5 Director of Legal and Regulatory Compliance

The Director of Legal and Regulatory Compliance has the responsibility to:

- Provide advice upon request to the Institutional Official, IRB, and other individuals involved with the Human Research Protection Program regarding the interpretation and application of federal and Louisiana state law relevant to human subject research and as an initial point of contact about the laws of other jurisdictions where research is conducted as they may apply to human subject research.
- Determine who meets the definition of "legally authorized representative" and "children" when human research is conducted in jurisdictions not covered by policies and procedures in accordance with applicable law.
    - Resolve conflicts among applicable laws

1.5.6 Sponsored Project Services

The Sponsored Project Services (SPS) has the responsibility to review contracts and funding agreements for compliance with Human Research Protection Program policies and procedures.

For both sponsored and non-sponsored human research this Institution abides by its ethical principles, applicable regulatory requirements, and its policies and procedures.

SPS reviews all research funding agreements with federal, foundation, non-profit, and industry sponsors. This institutional review ensures that all terms of an award or a contract are in compliance with institutional policies, including the policies of the HRPP. Only designated senior level individuals within the institution have the authority to approve sponsored research proposals and to execute research agreements on behalf of the institution.

When the grant or contract or other agreement includes human subject research activities that will be conducted by investigators who are not employees or agents of the institution, a subcontract is executed between this institution and the collaborating institution. The collaborating institution must also ensure that key personnel involved in human subject research are in compliance with the NIH policy on education in the protection of human research subjects and provide documentation of education of key personnel to the institution.

SPS, License and Technology Officer, the IRB and the Director of Legal and Regulatory Compliance meet on a regular basis to ensure consistency and communication about key issues in the protection of human subjects as they may impact the work, and specifically the research agreements, negotiated by Sponsored Human Research.

1.5.7 Pharmacy

The Pharmacy is available to provide guidance to investigators in relation to the management of the study drugs. The Pharmacist assures that information about all studies involving the use of drugs in the research is shared with the Pharmacy Staff as appropriate. Generally, responsibility for drug/biologic control and accountability is delegated to the Pharmacy by the investigator. Research involving administration of a test article that is not being stored, dispensed and managed by the Pharmacy requires protocol specific approval of the investigator’s plan to control the test article by IRB.

1.5.8 Research Computing Group (RCG)

The Research Computing Group (RCG) is a unit within the department of Computing Services. RCG's primary responsibility is the continuing development of a proprietary web-based portal to the clinical research database. The clinical research database is a Microsoft SQL Server database secured on the Pennington Biomedical network. Direct access to this database is restricted to authorized personnel within the RCG and Computing Services. Security is managed by the Pennington Biomedical Computing Services Infrastructure Security Group and is administered in accordance with established standard operating procedures. Active Directory (AD) credentials serve to authenticate, authorize and facilitate accountability for a user's access to PBRC information systems. The RCG team interfaces with researchers to ensure the efficient and accurate transfer of data from observation to electronic files for storage and analysis; monitors the data processing throughout each study's duration; and provides investigators with study specific data sets via web-based desktop data access. The team has developed custom applications for expedited creation of study specific data sets that may contain both PBRC data and Non-PBRC data. This development and data storage paradigm allows the team to work with both intramural and extramural researchers.

Guidelines for Good Clinical Practices as they relate to data handling have been documented and implemented in daily tasks. The group maintains current HIPAA Security Rule training and works closely with the Director of Legal and Regulatory Compliance.

1.5.9 Recruiting

Recruitment services for clinical trials conducted at The Pennington Biomedical Research Center (PBRC) are coordinated by the Recruitment Core. The Recruitment Core manages all incoming calls to determine study eligibility. Incoming calls are directed to a call center that is operated by 3 full time recruiters and is equipped with a Uniform Call Distributor (UCD) system. A UCD system expands the capability of a traditional phone system and allows multiple individuals to call simultaneously and be directed to the next available recruiter. The core utilizes an electronic message tracking application that tracks the outgoing phone call activity and a "smart" electronic phone screen system that screens potential participants upon initial phone contact and seamlessly matches them to alternative studies when deemed ineligible for the original study that the participant called. In 2012 the core launched a new web-screener for participants to be able to go on-line, choose a study that are interested in and complete a preliminary screening. The system is able to tell the participant upon completion whether they are eligible to that point in the screening

process and if they are ineligible the screener will alert them to other studies that they might be eligible for and at that point could continue to screen for those studies. If the participant is eligible they are then contacted by a live recruiter to complete the screening process and schedule their first screening appointment. All the information provided to the recruiter by the participant or the parent/guardian is protected in the Clinical Trials Database. The information is HIPAA protected and monitored by IT systems to assure no data breach occurs.

1.5.10 License and Technology

The Office of Intellectual Property and Technology Transfer is responsible for managing the intellectual property assets of the institution. Of particular relevance to human subject research protections are:

- Material Transfer Agreements (MTA's) – these are contracts that govern the transfer of tangible research materials between institutions for use in research. The Protocol Application asks whether tissues are to be distributed as part of such an agreement.

1.5.11 Institutional Biosafety Committee

The Institutional Biosafety Committee (IBC) ensures that research involving biological agents of humans, animals and plants, and/or recombinant DNA technology is conducted within existing Federal and State laws and guidelines. The IBC is obligated to require information from the Principal Investigator for a thorough review of proposed research. Reciprocal communication between the IRB and the IBC is essential in order to fulfill its functions relative to human research. The IRB shall not grant final approval of human participant research for those projects under purview of IBC, for example research involving recombinant DNA, gene transfer, microorganisms, viruses or biological toxins, until the project has been reviewed and approved by the IBC.

1.5.12 Radiation Committee

The Radiation Safety Committee (RSC) oversees the use of radioactive materials and radiation-producing devices at the institution. In collaboration with LSU, the committee promotes radiological safety through safety training, professional guidance, and technical support, in accordance with federal and state regulations and institutional policies. All human subject research involving radiation must have RSC approval before research activities may commence. Examples of uses of these sources include (but are not limited to) chest x-rays, DXA scans, CT scans, fluoroscopy, and nuclear medicine procedures. If radioactive isotopes are

administered to humans, the RSC and the RDRC (radioactive drug research committee) must provide approval before research activities may begin.

1.5.13 Clinics (Outpatient, Inpatient, TREC)

The Clinical Trials Unit (CTU) includes the inpatient, outpatient, pediatric and interventional research functions. Under the direction of the Principal Investigator, the CTU completes all clinical, medical and interventional procedures and processes as defined by the study protocol in compliance with all Institutional policies and procedures. The CTU works with the Principal Investigators to ensure the required resources necessary for study implementation and ongoing operation are available and meet specified study criteria.

The Clinical Trials Unit works closely with the Principal Investigators to ensure effective, accurate, and timely communication is maintained with the HRPP office to include, but not limited to, approval and modification of protocols and informed consents, reporting of Serious Adverse Effects (SAE), reporting of protocol deviations, changes in study status, changes in study personnel, and all other reports defined by the Institutional policies and procedures.

All staff completes the required initial and maintenance compliance training as defined by Institutional and Clinical Trials Unit policies and procedures. In-service training is provided to all staff as required based upon the development of new policies and procedures or changes in established policies and procedures.

1.6 Education and Training

IRB members, IRB staff, and others involved in the review of human research must complete CITI IRB Administration training. This training is valid for a three-year period, after which time CITI training must be completed again. IRB staff also train IRB members on the SOPs and forms applicable to IRB members including regulatory and guidance requirements noted in the section “Other Requirements (section 1.4.3).”

Investigators and research staff must complete CITI training relevant to the type of research being conducted.in accordance with PBRC policy 106. The IRB is notified electronically when CITI training is completed and notified by the Director of Legal and Regulatory Compliance of any investigator and research staff out of compliance with the policy.

1.7 Resources for the HRPP

Resources for the HRPP components are provided through the annual budget review processes in the administrative units in which the components reside.

The need for study-specific resources is evaluated at the local level. Investigators and sponsoring units are responsible to ensure that sufficient resources are allocated to all projects, whether sponsored or investigator-initiated. These include staffing and personnel (in terms of availability, number, expertise and experience); psychological, social and medical services (including counseling or social support services that may be required because of participation in a study); psychological, social, or medical monitoring, ancillary care, equipment needed to protect participants, and resources for participant communication. Study-specific resources are verified electronically as defined by Policy 301.00 Clinical Study Budget, Resource Facilitation and Initiation.

The need for incremental or off-cycle resources may emerge as a result of special or unusual demands on the offices, either as reported by the offices or by quality assurance/review activities, or through deliberations by the Executive Director.

Resources for the HRPP are allocated to the individual PBRC entities engaged in human-subjects research overseen by the HRPP. Such resources include, but are not limited to:

- Staffing commensurate with the size and complexity of the research program.
- Appropriate office space, equipment, material, and technology.
- Resources for the production, maintenance, and secure storage of HRPP and IRB records.
- Resources for auditing and other compliance activities and investigations of non-compliance.
- Access to legal counsel.
- Support for educational opportunities related to human research protections for IRB members, relevant administrative staff, and all members of the research team.
- Support for evaluation of Conflict of Interest; and
- Support for Community Outreach

1.8 Questions and Additional Information for the IRB

The IRB Office wants your questions, information, and feedback.

Contact and location information for the IRB Office is:
Human Research Protections Program Director
Pennington Biomedical Research Center
6400 Perkins Road

Baton Rouge, LA 70808
Email: irb@pbrc.edu
Phone: (225) 763-2693

1.9 Reporting and Management of Concerns

Questions, concerns, complaints, allegations of undue influence, allegations or findings of non-compliance, or input regarding the Human Research Protection Program may be reported orally or in writing. Employees are permitted to report concerns on an anonymous basis. Concerns may be reported to the IRB Chair, IRB Office, Institutional Official or Director of Legal and Regulatory Compliance.

The IRB has the responsibility to investigate allegations and findings of non-compliance and take corrective actions as needed. The Institutional Official has the responsibility to investigate all other reports and take corrective actions as needed.

Employees who report in good faith possible compliance issues should not be subjected to retaliation or harassment as a result of the reporting. Concerns about possible retaliation should be immediately reported to the Institutional Official or designee.

To make such reports, contact:
John P. Kirwan, Ph.D.
Executive Director
Pennington Biomedical Research Center
6400 Perkins Road
Baton Rouge, LA 70808
Email: John.Kirwan@pbrc.edu
Phone: (225) 763-2513

1.10 Monitoring and Auditing

In order to monitor and ensure compliance, internal or external auditors who have expertise in federal and state statutes, regulations and Institutional requirements will conduct periodic audits. Audits may focus on areas of concern that have been identified by any entity, i.e., federal, state or Institutional. Random audits may also be conducted. See HRPP policy 13.0 – Quality Improvement in the HRPP Program

1.11 Disciplinary Actions

The Institutional Official may place limitations or conditions on an investigator's or research staff's privilege to conduct human research whenever, in the opinion of the

Institutional Official, such actions are required to maintain the Human Research Protection Program.

1.12 Approval and Revisions to the Plan

This Human Research Protection Program Policy is to be approved by the Policy Committee of Pennington Biomedical Research Center. This policy is intended to be flexible and readily adaptable to changes in regulatory requirements. The Institutional Official has the responsibility to review this plan to assess whether it is providing the desired results. At the request of the HRPP Office or the Institutional Official, the Policy Committee has the authority to amend this plan as deemed necessary.

302.1 Addendum to Human Research Protections Program Policy

1.1 Investigators as Study Participants (Self-Experimentation)

Federal regulations require investigators to personally conduct or supervise research investigations. In cases where investigators are enrolled in their own trial, there exists an inherent conflict in reporting unanticipated events and ensuring data integrity with the degree required for credible investigations. In addition, it is possible that the ideation of a novel concept may outweigh an investigator's concern for his or her personal welfare. In light of these potential ethical issues, Pennington Biomedical Research Center does not allow an investigator to enroll in a research study in which he or she is an investigator.

2.0 Institutional Review Board

2.1 Policy

Pennington Biomedical Research Center has one IRB to ensure the protection of human subjects in research.

- IRB – Biomedical (IRB 00000708) (IORG00006218)
  The IRB is delegated to review human subject research for the following areas:
  - clinical trials such as drug studies.
  - research involving the social sciences.
  - prevention, treatment, or understanding of diseases.
  - research involving medical interventions.

All non-exempt human research subjects must be reviewed and approved by Pennington Biomedical Research Center IRB or a single Institutional Review Board (sIRB) for multi-center research prior to initiation of research activities. Refer to the HRPP policy 21.0 for information related to single IRB research.

Regulations & Guidance: DHHS 45 CFR 46.103

2.2 IRB Authority

Pennington Biomedical Research Center policy authorizes the IRB to:

a) Approve, conditionally approve (minor modifications required), withhold approval (major modifications required or major clarifications), or disapprove all research activities overseen and conducted at this Institution.
b) Suspend or terminate approval of research not being conducted in accordance with the IRB requirements or has been associated with unexpected serious harm to subjects; and
c) Observe, or have a third party observe, the consent process and the conduct of the research.
d) Request a directed audit; or otherwise investigate, address, remedy and, when required or appropriate, report on incidences of noncompliance with legal, regulatory, or IRB requirements or determinations; and
e) Conduct reviews and inquiries regarding human-subjects research as needed to obtain information necessary for the fulfillment of human research protection responsibilities and, for federally funded research, the institutional responsibilities outlined in the institutions' Office for Human Research Protections (OHRP)-approved Federal Wide Assurance (FWAs).

The IRB is responsible for reviewing research to ensure the protection of rights and welfare of human research subjects. It discharges this duty by complying with the requirements of the Common Rule and other applicable federal regulations; state laws and regulations; the terms of institutions' FWA; and institutional policies. Research that has been reviewed and approved by the IRB may be subject to further review and suspension and disapproval by the Institutional Officials consistent with Pennington Biomedical Research Center policy (see HRPP Policy 3 – IRB Review Process). However, such officials may not approve research that has not been approved by the IRB.

The IRB has the authority within the institution to determine:

- whether a research activity involves human subjects within the meaning of the DHHS, FDA, or other applicable federal regulations.
- whether a research activity involving human subjects is exempt from 45 CFR 46 and 21 CFR 56.

Investigators or others within the organization may not independently make exemption determinations.

Regulations & Guidance: DHHS 45 CFR 46.112; FDA 21 CFR 56.103; 21 CFR 56.109; 21 CFR 56.112; and 21 CFR 56.113.

2.3 Roles and Responsibilities

2.3.1 IRB Chair

The Executive Director of Pennington Biomedical Research Center appoints an IRB Chair to serve for unlimited terms on the IRB. Any change in appointment, including re-appointment or removal, requires written notification from the Executive Director.

The IRB Chair should be a highly respected individual, fully capable of managing the IRB, and the matters brought before it with fairness and impartiality. The task of making the IRB a respected part of the Institution will fall primarily on the shoulders of the IRB Chair. The IRB must be perceived to be fair, impartial, and immune to pressure by the Institution's administration, the Investigator whose protocols are brought before it, and other professional and nonprofessional sources.

The criteria used to select an IRB Chair include experience with, and knowledge of, applicable federal and state laws and regulations, and Institutional policies. This individual must be willing to commit to the IRB; must have experience as an IRB member; and must demonstrate excellent communication skills, along with an

understanding of clinical research. The IRB Chair must also be flexible and demonstrate a thorough understanding of ethical issues involved in clinical research.

The IRB Chair convenes and chairs the meetings of the IRB and is required to attend a majority of the convened meetings of the IRB. The IRB Chair may conduct, or delegate expedited review of research that qualifies for such review; review the responses of Investigators to contingencies of the IRB (to secure IRB approval); and to review and approve minor changes in previously approved research during the period covered by the original approval.

The IRB Chair may delegate such authority to another experienced IRB member. The IRB Chair ensures that membership of the IRB is recruited, appointed and oriented such that the IRB is duly qualified to fulfill its obligations to review, require modifications to approve (or disapprove) research protocols that represent the breadth of research submitted to the IRB by Pennington researchers. The IRB Chair maintains a working knowledge of federal human subject's regulations through continued education and training. The IRB Chair attends institutional meetings that involve the HRPP/IRB office. The IRB Chair participates in Subcommittees.

The IRB Chair is a voting member and is the signatory for correspondence generated by the IRB and may delegate signatory authority to another experienced IRB member.

The performance of the IRB Chair will be reviewed on an annual basis by the Executive Director or designee. If the IRB Chair is not functioning in accordance with the IRB's mission, policies and procedures; has an undue number of absences; or is not fulfilling the responsibilities of IRB Chair, then he/she will be removed by the Executive Director and replaced by a suitable alternative. The periodic assessment provides feedback to IRB chair, and vice-chair when appropriate.

2.3.2 IRB Co-Chair

The responsibilities of the Co-Chair mirror those of the Chair with the extent of responsibilities outside the meeting dependent on the activities delegated by the Chair and ability of the Chair to perform those duties (e.g., due to vacation, illness, leave of absence), including:

- Preside over meetings of the fully convened IRB and ensure that the IRB carries out its duly authorized responsibilities as required by federal regulations, ethical principles, state laws and HRPP policy.
- Review and approve protocol submissions that qualify for expedited review pursuant to federal regulations, ethical principles, state laws and University policies.

- Ensure that membership of the IRB is recruited, appointed and oriented such that the IRB is duly qualified to fulfill its obligations to review, require modifications to approve (or disapprove) research protocols that represent the breadth of research submitted to the IRB by Pennington researchers.
- Maintain a working knowledge of federal human subject's regulations through continued education and training.
- Attend institutional meetings that involve the HRPP/IRB office
- Participate in Subcommittees.
- Represent the IRB at national and local meetings related to institutional review board activities and human subject protections.

The performance of the IRB Co-Chair will be reviewed on an annual basis by the Executive Director or designee. If the IRB Co-Chair is not functioning in accordance with the IRB's mission, policies and procedures; has an undue number of absences; or is not fulfilling the responsibilities of IRB Co-Chair, then he/she will be removed by the Executive Director and replaced by a suitable alternative. The periodic assessment provides feedback to IRB chair, and vice-chair when appropriate.

2.3.3 HRPP/IRB Staff

2.3.3.1 HRPP Director

The HRPP Director supervises the Human Research Protections Program. The HRPP Director is the primary contact and liaison at the Institution for communications with Federal, State and local regulatory agencies with respect to Human Subjects (e.g., OHRP or the FDA). The HRPP Director responds to faculty and staff questions about Human Subjects Research as well as organizing and documenting the IRB review process. The HRPP Director works closely with the IRB Chair and others within the HRPP in the development, management and implementation of IRB policy and procedures to ensure compliance with all local, state, and federal regulations governing human research protections. This includes monitoring changes in regulations and external policies and emerging ethical and scientific issues that relate to human research protection. The HRPP Director is not a voting member of the IRB.

2.3.3.2 IRB Manager

The IRB Manager manages all day-to-day operations of the IRB office. Assesses minutes for quality, completeness, and regulatory compliance and IRB member reviews for quality, completeness, and regulatory compliance. The IRB Manager analyzes overall findings for trends and key process failures, providing input for team training regarding identified quality trends. Participates in and

provide support during preparation for and conduct of internal and external quality audits of PBRC. Contributes in making not human subject or exempt determinations and approving minor expedited submissions as allowed by HRPP policy and authorized by the IRB Chair. The IRB Manager provides guidance to researchers on IRB policies and assist investigators and research staff with protocol and consent requirements for IRB submission. Works in partnership with the HRPP Director, the IRB Chair and others to develop written guidelines to improve communication and understanding of human research requirements. Assist in the maintenance of the HRPP website as needed. The IRB Manager is a voting member of the IRB.

2.3.3.3 IRB Coordinator

The IRB Coordinator organizes IRB meetings and review activities: prepares relevant materials and necessary correspondence, including agendas and reports. Reviews project submissions for completeness; communicates with investigators and coordinators for any additional information or materials. Prepares and enters information into database for new submissions. Prepares appropriate paperwork and approval correspondence in conjunction with submissions to the IRB; communicates with investigators and coordinators for additional information or materials. Updates and maintains records related to IRB membership, maintains various tracking logs and files related to IRB activities. The IRB Coordinator maintains records of IRB approvals and oversees the archiving of terminated IRB files and responds to general information queries from investigators and study coordinators regarding IRB procedures. Assists HRPP Director and IRB Manager with administrative tasks as needed and maintains a good working relationship with IRB members, Principal Investigators, Project Managers, and Study Coordinators

2.4 IRB Membership

IRB members are selected based on appropriate diversity, including consideration of race, gender, and cultural backgrounds; varied community involvement and affiliations; knowledge and experience with vulnerable populations; and with multiple, diverse professions or specialties, including both scientific members and non-scientific members. The structure and composition of the IRB must be appropriate to the nature of the research that is reviewed. Every effort is made to have member representation that has an understanding of the areas of specialty that encompasses the types of research performed at the Institution. Pennington Biomedical Research Center has procedures (see section 2.7, Use of Guests & Consultants and Scientific Merit section in Policy 3) that specifically outline the requirements for protocol review by individuals with

appropriate scientific or scholarly expertise beyond or in addition to that available through the IRB members.

In addition, the IRB will include members who are knowledgeable about and experienced in working with vulnerable populations (e.g., children, pregnant women, economically or educationally disadvantaged persons or individuals with impaired decision-making capacity) that typically participate in research.

The IRB must promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects and possess the professional competence necessary to review specific research activities. Ideally, a single member of the IRB could exhibit a profile that fulfills multiple specific requirements for IRB composition.

Regulations & Guidance: DHHS 45 CFR 46.107; FDA 21 CFR 56.107

A. Definitions

Affiliated IRB Member: is an employee or agent of Pennington Biomedical Research Center or affiliated with Pennington Biomedical Research Center (faculty or medical staff). If a member of that person's immediate family is affiliated with Pennington Biomedical Research Center, then the IRB member must disclose this information. Affiliated members include but are not limited to individuals who are: full or part-time employees; members of any governing panel or board of the Institution; paid or unpaid consultants; and volunteers working at the Institution on business unrelated to the IRB.

Experienced Member: is an IRB member determined by the IRB Chair to be qualified to perform reviews using expedited procedures. The following criteria are considered when determining whether an IRB member is experienced: length of IRB service, training regarding expedited review procedures, research experience/expertise, and/or work with the research participants being studied.

Non-Affiliated Member: is an IRB member with no affiliation to the Institution, nor can any immediate family member be affiliated with the Institution. The non-affiliated member is drawn from the community and must be willing to discuss issues and research from that perspective.

Alternate Member: is an individual who has the experience, expertise, background, professional competence, and knowledge comparable to that of the primary IRB member(s) whom the alternate would replace.

Non-scientific Member: is any IRB member who has formal education and training in a discipline generally considered to be non-scientific (e.g., humanities, law,

business) and/or is engaged in an occupation or role that is generally considered to be non-scientific (e.g., law enforcement, minister).

Scientific Member: is an individual who has formal education and training as a physician or other medical professional, and M.S. and/or Ph.D. level physical, biological, or social behavioral scientists.

B. Composition of the IRB

a. The IRB will have at least five members with varying backgrounds to promote complete and adequate review of research activities commonly conducted by the Institution.
b. The IRB will be sufficiently qualified through the experience, expertise, and diversity of its members, including consideration of race, gender, cultural backgrounds and sensitivity to such issues as community attitudes, to promote respect for its advice and counsel in safeguarding the rights and welfare of human subjects.
c. In addition to possessing the professional competence necessary to review specific research activities, the IRB will be able to ascertain the acceptability of proposed research in terms of Institutional policies and regulations, applicable law, and standards of professional conduct and practice. The IRB will therefore include persons knowledgeable in these areas.
d. If the IRB regularly reviews research that involves a vulnerable category of subjects, consideration will be given to the inclusion of one or more individuals on the IRB, who are knowledgeable about and experienced in working with these subjects. When protocols involve vulnerable populations, the review process will include one or more individuals who are knowledgeable about or experienced in working with these subjects, either as members of the IRB or as consultants (see Consultant - Vulnerable Populations section in Policy 3 and Policy 6 - Vulnerable Subjects in Research).
e. Every nondiscriminatory effort will be made to ensure that the IRB does not consist entirely of men or entirely of women, including the Institution’s consideration of qualified persons of both sexes. The IRB shall not consist entirely of members of one profession.
f. The IRB includes at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in non-scientific areas.
g. At least one member who is not otherwise affiliated with Pennington Biomedical Research Center and who is not part of the immediate family of a person who is affiliated with Pennington Biomedical Research Center.
h. One member may satisfy more than one membership category.

i. The IRB has at least one member who represents the perspective of research subjects. At PBRC, the non-scientist member serves in this capacity.

Regulations & Guidance: DHHS 45 CFR 46.107; FDA 21 CFR 56.107

C. Appointment of New IRB Members

The IRB Chair, in coordination with the HRPP Director, is responsible for selecting individuals to serve as a new IRB member (and indicate whether regular or alternate). However, the Institutional Official makes the final determination and appointment regarding new IRB members.

Initial appointments are made for a year service term and IRB members are evaluated annually for extension of appointment. Any change in appointment or removal by the IRB Chair, requires written notification. Members may resign by written notification to the IRB Chair.

D. Documentation and Information for New IRB Members

The following items are required from each member of the IRB at initial appointment and as directed and will be made available as appropriate, upon request [DHHS 45 CFR 46.107]:

- Current curriculum vitae (“CV”) annually.
- Participation in the required initial education (section 2.10 B) and new IRB member orientation (section 2.10 A) must occur prior to review of any research.
- Documentation of current Institutional certification in compliance education (e.g., CITI Training). The IRB office documents and files compliance training for IRB members.
- Members must make every effort to attend all meetings for which the member is scheduled. (see section 2.8 - Duties of IRB Members)
- All members must sign a Confidentiality Agreement upon assignment as a member which is effective for the duration of the term served regardless of the length of the term. A Conflict-of-Interest Disclosure must be completed and signed annually.
- Documents supporting final appointments along with records of continuing education will become part of the permanent membership records maintained by IRB office. The IRB membership requires annual evaluation. Required changes will be reported to the OHRP.
- A list of IRB members and their qualifications are maintained.

E. Periodic Review of IRB Composition and Membership

On an annual basis, the IRB Chair shall review the membership and composition of the IRB to determine if they continue to meet regulatory and Institutional requirements. Required changes in IRB members will be reported to the OHRP.

2.5 Alternate IRB Members

The appointment and function of alternate members is the same as that of regular IRB members; and the alternate's expertise and perspective are comparable to those of the regular member. The area of expertise of the alternates should match that of the regular member such that the federal policy requirements are met if a regular member cannot attend an IRB meeting. The role of the alternate member is to serve as a voting member of the IRB when the regular member is unavailable to attend a convened meeting. When an alternate member substitutes for a primary member, the alternate member will receive and review the same materials prior to the IRB meeting that the regular member received or would have received.

The IRB roster identifies the regular member(s) for whom each alternate member may substitute. The alternate member will not be counted as a voting member unless the regular member is absent. The IRB minutes will document when an alternate member has replaced a regular member.

2.6 IRB Member Conflict of Interest

No IRB member may participate in the review (initial, continuing review, modification, unanticipated problem or non-compliance) of any research project in which the member has a conflict of interest ("COI"), except to provide information as requested. Matters involving financial COI involving IRB members are governed by the Institution's policy detailed in Pennington Biomedical Research Center Policy 401.00 Individual Financial Conflicts of Interest Policy, IRB members may find themselves in any of the following COI when reviewing research:

1. Where the member or consultant is involved in the design, conduct, and reporting of the research.
2. Where an immediate family member of the member or consultant is involved in the design, conduct, and reporting of the research.
3. Where the member holds significant financial interests related to the research being reviewed; and
4. Any other situation where an IRB member believes that another interest conflicts with his or her ability to deliberate objectively on a protocol. For expedited reviews all reviewers must attest on the expedited reviewer form whether a COI exists. If a COI exists, a member is asked to notify the IRB immediately, so the review can be re-assigned.

It is the responsibility of each IRB member to disclose any COI with a study submitted for review and recuse him/herself from the deliberations and vote by leaving the room, which departure is noted in the minutes. Only those IRB members who are independent of the investigator and the sponsor of the trial should vote/provide opinion on a trial-related matter.

The IRB Chair will poll IRB members at each convened meeting to determine if a COI exists regarding any protocols to be considered during the meeting and reminds the committee that members with conflicts should recuse themselves by leaving the room during the deliberation and vote of a specific protocol. IRB members with a conflicting interest are excluded from being counted towards quorum. All recusals by members with COI are recorded in the minutes.

IRB members with a conflict are documented in the minutes as being absent with an indication that a conflict of interest was the reason for the absence.

If the conflict-of-interest status of an IRB member changes during the course of a study, the IRB member is required to declare this to the IRB Chair.

Regulations & Guidance: DHHS 45 CFR 46.107(d); FDA 21 CFR 54; 21 CFR 56.107(e)

2.7 Use of Guests and Consultants

At the discretion of the IRB, the Principal Investigator may be invited to the IRB meeting to answer questions about their proposed or ongoing research. The Principal Investigator may not be present for the discussion or vote on their research.

A consultant is an individual with competence in a special area that the IRB has invited to assist in the review of issues which require expertise beyond or in addition to the availability on the IRB. These individuals do not count for IRB quorum purposes and cannot vote on any issue before the IRB [45 CFR 46.107((e)].

When necessary, the IRB Chair may solicit advice or otherwise engage individuals to assist the IRB in its review of issues or IRB proposals, which require appropriate scientific or scholarly expertise beyond or in addition to that available on the IRB.

The need for an outside reviewer is determined in advance of the IRB meeting by the IRB Chair by reviewing the IRB proposals scheduled to be reviewed at the convened meeting. The IRB staff will ensure that all relevant materials are provided to the outside reviewer prior to the convened IRB meeting.

Outside reviewers or consultants can be obtained either within or outside the Pennington Biomedical Research Center. In the event that additional scientific or scholarly expertise cannot be obtained for a research proposal the IRB Chair will defer the proposal to the next IRB meeting in order that appropriate review may be obtained.

Consultants are subject to the policy on conflicts of interest for IRB members and will sign a Financial Disclosure form. Consultants must remain in compliance with the COI policy. Individuals who have a COI or whose spouse or family members have a COI in the research will not be invited to provide consultation. Consultants with a conflict are documented in the minutes as being absent with an indication that a conflict of interest was the reason for the absence.

The consultant's findings will be presented to the convened IRB for consideration either in person or in writing. If in attendance, these individuals will provide consultation but may not participate in or observe the vote.

Ad hoc or informal consultations requested by individual IRB members (rather than for convened IRB review) will be requested in a manner that protects the researcher's confidentiality and follows the COI policy.

To the extent that written statements or recommendations are provided by a consultant, a copy will be kept in IRB records. Key information provided by consultants at meetings will be documented in the minutes. Written reviews provided by the outside reviewer will be filed with the protocol. If a consultant is obtained, the consultant will be required to complete the same review documentation required by IRB members for appropriate review of a submission.

Regulations & Guidance: DHHS 45 CFR 46.107(e); FDA 21 CFR 56.107(f)

2.8 Duties of IRB Members

Except for emergency IRB meetings, the agenda, submission materials, proposals, proposed informed consent forms and other appropriate documents are distributed to IRB members approximately one week prior to the convened meetings at which the research is scheduled to be discussed. For emergency IRB meetings, these written materials will be submitted as timely as possible in advance of the scheduled IRB meeting date and time. IRB members will treat the IRB proposals, protocols, and supporting data confidentially. All copies of the protocols and supporting data are returned to the IRB staff at the conclusion of review for document destruction.

Unaffiliated members must attend at least 60% of the IRB meetings (for which the member is scheduled) during a calendar year. The member is to contact the IRB office of any potential absence as far in advance as possible; an unaffiliated member who repeatedly misses meetings (>60% without prior notice or excuse) may either be asked to step down or have an alternate assigned who can act in his/her stead.

2.9 Attendance Requirements

IRB members should attend all meetings for which they are scheduled. If a member is unable to attend a scheduled meeting, they should timely inform the IRB Chair or IRB staff member at least one week prior to the scheduled meeting. In the case of an emergency, members should provide notification as soon as possible. If an IRB member is unable to attend IRB meetings for a prolonged period, then such notice should be given so that the IRB Chair can determine whether an alternate member is needed and, if so, such alternate member should be temporary or permanent. If an IRB member is to be absent for an extended period, such as for a sabbatical, he or she must notify the IRB at least 30 days in advance so that an appropriate replacement can be obtained. The replacement can be temporary, for the period of absence, or permanent if the member is not returning to the IRB. If the member has a designated alternate (see sections 2.4 and 2.5), the alternate can serve during the regular member's absence, provided the IRB has been notified in advance.

Designated alternates (alternate voting members) shall be asked to attend meetings and vote when the primary voting member indicates that s/he does not plan to attend the meeting. Should both the primary voting member and alternate voting member attend the same meeting and be present for review of the same research activity, only one member shall vote on the specific research activity under review. The other shall be recorded in the minutes as attending, but not voting on the research activity.

The Chair of the IRB may recommend suspension or removal for cause of any IRB member; provided, however, that such member shall have been given reasonable notice of the grounds for the suspension or removal and an opportunity to be heard. For this purpose, cause (with respect to a voting member) shall include the failure to attend at least 60% of the convened meetings in a calendar year of the IRB panel of which he/she is a member without excuse or the failure to perform reviews when assigned as a primary or secondary reviewer without prior notice or excuse.

2.10 Training & Education

Pennington Biomedical Research Center is committed to providing initial and on-going training and education for the IRB Chair, IRB members, and IRB staff related to

research ethics concerns. The IRB Chair, IRB members and IRB staff are subject to the Institutional Policy 106.00 for training and education requirements.

A. New IRB Members—Orientation

New IRB members, including alternate members, will meet with the HRPP Director for an informal orientation session. At the session, the new member will be given copies of the following:

- Pennington Biomedical Research Center IRB 101 Presentation
- Pennington Biomedical Research Center IRB Policies and Procedures
- IRB member Reviewer forms
- The Belmont Report
- Applicable federal and state regulations including
    - 45 CFR Part 46 – The Common Rule
    - 21 CFR Part 50 – Protection of Human Subjects
    - 21 CFR Part 56 – Institutional Review Boards

B. New IRB Members—Initial Education

Before serving as a primary reviewer, a new IRB member must receive and successfully complete the education requirement.

C. IRB Members—Continuing Education

To ensure that oversight of research involving human subjects is ethically grounded and the decisions made by the IRB is consistent with current regulatory and policy requirements, training is continuous for IRB members throughout their service on the IRB. Educational activities include, but are not limited to:

- In-service training at IRB meetings
- Distribution of appropriate publications; and
- Identification and dissemination by the HRPP Director of new information that might affect the IRB, including laws, regulations, policies, procedures, and emerging ethical and scientific issues to IRB members via e-mail, mail, or during IRB meetings.

2.11 Insurance Coverage for Research Oversight Activity

Non-Pennington employees are appointed members of the Pennington Biomedical Research Center, for the sole purpose of their activities as members of the IRB. In this way, they, along with Pennington Biomedical Research Center employees, are protected by the Louisiana State University System Office of Risk Management.

2.12 Review of IRB Member Performance

IRB member's performance will be reviewed on an annual basis. The HRPP Director, in coordination with the IRB Chair, will use the IRB member self-assessments to evaluate each member. IRB members who are not acting in accordance with the IRB mission or IRB policies and procedures, or who have an undue number of absences will be removed. The periodic assessment provides feedback to IRB members when appropriate.

3.0 IRB Review Process

3.1 Policy

All human subjects' research in the Institution must meet the criteria for one of the following methods for review:

- Exempt review
- Expedited review
- Full review by a convened IRB

The IRB will ensure that the research meets all required ethical and regulatory criteria for initial, continuing review and any modifications of approved research.

The following describe the procedures required for the review of research by the IRB.

3.2 Human Subjects Research Determination

Investigators relying on the institution for IRB review of human subjects research are required to complete an IRB application to receive confirmation that an activity does not constitute human subjects. The IRB Chair or designee is responsible for making determinations of exemption from the requirements of federal regulations on whether an activity constitutes human subjects research based on the definitions of human subjects research. The request must be made through IRBManager. All requests must include sufficient documentation of the activity to support a determination by the IRB.

Determinations as to whether an activity constitutes human subjects research will be made according to the Not Human Subjects Research submission form and using Decision Tree(s) at www.hhs.gov/ohrp/policy/checklists/decisioncharts.html. After a determination by the IRB Chair (or designee) that the project is not human subjects research, the Investigator is notified in writing.

Regulations & Guidance: DHHS 45 CFR 46.101 (pre-2018); 46.104 (2018 new common rule); FDA 21 CFR 56.101

3.3 Exempt Studies

Exempt research is subject to Institutional review and must be determined and acknowledged by the IRB Chair (or designee). The following sections will describe activity that is exempt and the procedures for conducting exempt review. Investigators will submit an Application for Initial Review and protocol to the IRB for an exempt

determination. After a determination that research is exempt the Investigator is notified in writing. The study is subject to a status report every five years; however, the Investigator is asked to let the IRB know when the study is closed.

Documentation of all exemption determinations made are recorded and maintained by the IRB office.

3.3.1 Limitations on Exemptions

- Exemption for research involving educational tests, survey, interview procedures or observations of public behavior does NOT apply to research in children, except for research involving observations of public behavior when the Investigator does not participate in the activities being observed. The exemption also does not apply to research involving children when information is recorded with identifiers or code linked to identifiers.
- Pennington does not conduct research involving prisoners. However, the exemptions do not apply to research involving prisoners except for research aimed at involving a broader subject population that only incidentally includes prisoners.
- Exempt research categories do not apply to research that involves FDA-regulated products (studies using investigational drugs, biologics, or devices for which the FDA has granted an investigational new drug [IND] or investigational device exemption [IDE], or non-significant-risk devices).

3.3.2 Categories of Exempt Research (Pre-Common Rule)

Unless an exception exists, the following categories of research below are considered exempt research and not regulated by the Common Rule or FDA regulations if approved prior to January 21, 2019.

1. Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as:
   a. Research on regular and special education instructional strategies, or
   b. Research on the effectiveness of, or the comparison among instructional techniques, curricula, or classroom management methods.
   [45 CFR 46.101(b) (1)]

2. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:
   a. Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and

   b. Any disclosure of the human subjects responses outside the research could reasonably place the subjects at risk of criminal or civil liability, loss of insurability or be damaging to the subject's financial standing, employability, or reputation [45 CFR 46.101(b)(2) or (b)(3)]

3. Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (2), if:
   a. The human subjects are elected or appointed public officials or candidates for public office; of
   b. Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter. Any disclosure of the human subjects responses outside the research could reasonably place the subjects at risk of criminal or civil liability, loss of insurability or be damaging to the subject's financial standing, employability, or reputation. [45 CFR 46.101(b)(2) or (b)(3)]

4. Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the Investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. [45 CFR 46.101(b) (4)]
   NOTE: In order to be eligible for this exemption, all of the materials have to exist at the time the research is proposed.

5. Research and demonstration projects which are conducted by or subject to the approval of federal department or agency heads, and which are designed to study, evaluate, or otherwise examine:
   a. Public benefit or service programs;
   b. Procedures for obtaining benefits or services under those programs;
   c. Possible changes in or alternatives to those programs or procedures; or
   d. Possible changes in methods or levels of payment for benefits or services under those programs.
   e. The program under study must deliver a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older American Act).
   f. The research demonstration project must be conducted pursuant to specific federal statutory authority, there must be no statutory requirements of IRB review, the research must not involve significant physical invasions or intrusions upon the privacy of subjects', and the exemption must be invoked only with authorization or concurrence by the funding agency.

6. Taste and food quality evaluation and consumer acceptance studies,
    a. If wholesome foods without additives are consumed; or
    b. If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the US. Department of Agriculture.

Regulations & Guidance: DHHS 45 CFR 46.101(b); 45 CFR 46.401(b); FDA 21 CFR 56.104(c)-(d); OHRP Guidance at 45 CFR 46.101(b) (5): Exemptions for research and Demonstration Projects on Public Benefit and Service Programs

In addition to the federal criteria for exemptions, this Institution evaluates whether the proposed research meets the Institution's ethical standards. The following ethical standards are reviewed on proposed research considered for an exemption:

- The research holds out no more than a minimal risk to participants
- The selection of subjects is equitable
- If there is a recording of identifiable information, there are adequate provisions to maintain the confidentiality of data.
- If there are interactions with participants, the IRB should determine whether there should be a consent process that will disclose such information as:
    - The activity involves research
    - A description of procedures
    - The participation is voluntary
    - The name and contact information of the researcher
- There are adequate provisions to maintain the privacy interests of participants.

When exempt research involves an interaction with participants, the reviewer will review the consent process to ensure that subjects are (1) informed that the activity is research and that their participation is voluntary; and (2) given a description of the research activity and the name and contact information for the investigator conducting the research. The reviewer uses checklists to document review and exemption determinations. The IRB notifies the PI in writing that the research is exempt and that the PI may not make changes to the research activity without first discussing the changes with the IRB to ensure that the changes are within the parameters for exemption. If the research no longer meets the criteria for exemption, the investigator must resubmit the research for review by the IRB at a convened meeting or using the expedited review procedure, whichever is appropriate to the research activities.

3.3.3 Categories of Exempt Research (New Common Rule)

Unless an exception exists, the following categories of research below are considered exempt research and not regulated by the Common Rule or FDA regulations if approved on or after January 21, 2019.

1. Research, conducted in established or commonly accepted educational settings, that specifically involves normal educational practices that are not likely to adversely impact students' opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.
   [45 CFR 46.101(b) (1)]

2. Research only includes interactions involving the use of educational tests, survey procedures, interview procedures or observation of public behavior (including visual or auditory recording), if at least one the following criteria is met:
   a. the information recorded cannot be readily linked back to the subjects in such a manner that subjects' identity can be readily ascertained, directly or through identifiers linked to the subjects; or
   b. any disclosure of this information would not place the subjects at risk of certain harms, or
   c. the information is recorded in an identifiable manner, even if sensitive, provided that an IRB determines through limited review that , when appropriate, there are adequate privacy and confidentiality protections in the study.
   d. any disclosure of the participants' responses outside the research would not reasonably place the participants at risk of criminal or civil liability or be damaging to the participants' financial standing, employability, educational advancement, or reputation.
   [45 CFR 46.101(b)(2)]

3. Research involving benign behavioral interventions through verbal, written responses, (including data entry or audiovisual recordings) from adults who prospectively agrees and one of the following is met:

   a. the information recorded cannot be readily linked back to the subjects in such a manner that subjects' identity can be readily ascertained, directly or through identifiers linked to the subjects;

b. any disclosure of the human participants' responses outside the research would not reasonably place the participants at risk of criminal or civil liability or be damaging to the participants' financial standing, employability, educational advancement, or reputation; or

c. If the research involves deception of participants regarding the nature or purposes of the research:

- The participant authorizes the deception through a prospective agreement to participate in research in circumstances in which the participant is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

Benign behavioral interventions are defined as "brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing."

Exemption 3 is not applicable to biomedical research. Additionally, it applies only to research with adults; it is not applicable to research with children. [45 CFR 46.101 (b)(3)]

4. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

    a. The identifiable private information or identifiable biospecimens are publicly available; or
    b. Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects; or
    c. The research involves only information collection and analysis involving the investigator's use of identifiable health information when that use is regulated by HIPAA [under 45 CFR parts 160 and 164, subparts A and E, for the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b);] or
    d. The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information

obtained for non-research activities if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501

Regulations [Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501]

5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs.

6. Taste and food quality evaluation and consumer acceptance studies:
    a. If wholesome foods without additives are consumed; or
    b. If a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the US. Department of Agriculture.

Exemption categories 7 and 8 do not apply to PBRC studies.

Regulations & Guidance: DHHS 45 CFR 46.101(b); 45 CFR 46.401(b); FDA 21 CFR 56.104(c)-(d); OHRP Guidance at 45 CFR 46.101(b) (6): Exemptions for research and Demonstration Projects on Public Benefit and Service Programs

In addition to the federal criteria for exemptions, this Institution evaluates whether the proposed research meets the Institution’s ethical standards. The following ethical standards are reviewed on proposed research considered for an exemption:

- The research holds out no more than a minimal risk to participants.
- The selection of subjects is equitable.
- If there is a recording of identifiable information, there are adequate provisions to maintain the confidentiality of data.

- If there are interactions with participants, the IRB should determine whether there should be a consent process that will disclose such information as:
    - The activity involves research.
    - A description of procedures.
    - The participation is voluntary.
    - The name and contact information of the researcher.
- There are adequate provisions to maintain the privacy interests of participants.

When exempt research involves an interaction with participants, the reviewer will review the consent process to ensure that subjects are (1) informed that the activity is research and that their participation is voluntary; and (2) given a description of the research activity and the name and contact information for the investigator conducting the research. The reviewer uses checklists to document review and exemption determinations. The IRB notifies the PI in writing that the research is exempt and that the PI may not make changes to the research activity without first discussing the changes with the IRB to ensure that the changes are within the parameters for exemption. If the research no longer meets the criteria for exemption, the investigator must resubmit the research for review by the IRB at a convened meeting or using the expedited review procedure, whichever is appropriate to the research activities.

Regulation (45CFR46.104)

3.3.4 Limited IRB Review

Limited IRB review is a process that is required only for certain exemptions and does not require an IRB to consider all the IRB approval criteria in §46.111. In limited IRB review, the IRB must determine that certain conditions, which are specified in the regulations, are met. Limited IRB review may be done via the expedited review mechanism, that is, by the Chair or an experienced IRB member designated by the Chair (although it can also be conducted by the full IRB).

The two exemptions that require limited IRB review at PBRC are exemptions (d)(2)(iii), (d)(3)(i)(C).

Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study are eligible for limited review: (A) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or (B) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care. [DHHS 45 CFR 46.104]

Written materials specify the information that researchers must submit for limited IRB review, including:

- The full protocol, application, or a protocol summary containing the relevant information to determine whether the proposed research fulfills the criteria for approval.

- Proposed consent document. Written materials specify that IRB members conducting limited IRB review may not disapprove research.

Written materials must specify the required determinations when conducting limited IRB review.

- For exemption Categories 2 and 3, there are adequate protections for privacy interests of participants and the confidentiality of identifiable data.
- The Institution evaluates whether the proposed research under limited IRB review meets the Institution's ethical standards.
- Continuing review is not required for studies that qualify for a limited review.
- PBRC retains the authority to suspend or terminate IRB approval of research approved with limited review.

3.3.5 FDA Exemptions

The following category of clinical investigation is exempt from the FDA requirements of IRB review:

- Taste and Food Quality Evaluations and Consumer Acceptance Studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the FDA or approved by the EPA or the Food Safety and Inspection Service of the U.S. DOA. [FDA 21 CFR 56.104(d)]

The exemption at 21 CFR 56.104(c) does not apply to human-subjects research regulated by the DHHS. FDA-regulated research determined to be exempt from 21 CFR 56 IRB requirements is subject to 21 CFR 50 Informed Consent of Human Subjects. When providing ethical review of exempt research, the reviewer is also responsible for determining that the research meets the institution's ethical principles for human subject protection, specifically the Ethical Principles and Guidelines for the Protection of Human Subjects of Research (the "Belmont Report") and the requirements of the Health Insurance Portability and Accountability Act (HIPAA) of 1996. Specifically, the IRB is responsible for determining that (1) the research presents no more than minimal risk to subjects; (2) the selection of subjects is equitable; and (3) if applicable, there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of identifiable data.

Clinical investigations governed by FDA regulations may only be determined to be exempt from IRB review/oversight if category 6 applies or in the case of emergency use.

3.4 Expedited Review

The IRB uses the expedited review procedure for review and approval of certain categories of human subjects research that involves no more than minimal risk and for review and approval of minor changes in approved research during the period of IRB approval [DHHS 45 CFR 46.110 and FDA 21 CFR 56.110].

When the IRB is not required to conduct continuing review (for studies approved under the new common rule), records must provide a rationale for any decisions to conduct done continuing review of research otherwise eligible for review using the expedited procedure.

The IRB Chair or designee may use expedited review procedures to approve a limited class of research activities involving human subjects. Expedited IRB review procedures may be used for the following:

- Initial or continuing review of specific categories of research not greater than minimal risk
- Continuing review of research previously approved by the convened IRB, under specified circumstances.
- Review of minor changes to previously approved research.

This policy describes the situations in which research may qualify for expedited review, as well as the process by which the IRB reviews research by expedited procedures.

When reviewing non-exempt human subjects research and clinical investigations using the expedited review procedure, the IRB Chair and designee are subject to the policy on IRB member conflicts of interest.

3.4.1 Definitions

Expedited Review: Process by which designated IRB members, on behalf of the full IRB, approve a limited class of research activities through reviews conducted outside of the convened IRB meeting.

Expedited Review is used by the IRB for either or both of the following:

- Some or all the research appearing on the list of categories of research eligible for expedited review and found by the reviewer(s) to involve no more than minimal risk; and/or

- Minor changes in previously approved research during the period (of one year or less) for which approval is authorized. (See section 3.4.2)

Minor changes: Research that in the judgment of the IRB does not affect the assessment of the risks and benefits of the study by substantially altering any of the following:

- The level of risk to subjects.
- The research design or methodology.
- The subject population.
- The qualifications of the research team.
- The facilities available to support the safe conduct of the research.
- Any other factor which would warrant review of the proposed changes by the convened IRB.

Examples of changes to previously approved research that may be considered minor (and may be reviewed using expedited procedures) when they do not alter the risk/benefit ratio include:

1. Changes in study documents, such as recruitment materials, consent forms, questionnaires, etc. that do not materially affect participation of the subject in the study or alter the meaning of the text (e.g., formatting, phone or room numbers, etc.).
2. Clarifications of the study protocol, procedures, or consent language that do not introduce new procedures or information.
3. Changes in wording or deletions of a question(s) on a survey or in the material properties of a stimulus, where the change or deletion does not alter the fundamental meaning of the item for the research or change the nature of the subject's participation in the study.
4. Addition of a standardized survey instrument that does not substantially increase risk to participants or the duration of their study participation.
5. Addition of advertisements or recruitment materials that do not pose undue influence and are easily compared to the approved informed consent script or document.
6. Increases in local site enrollment in multi-site studies where the increase does not exceed the approved total number of participants across all sites.
7. Decreases in number or frequency of data collection points that do not compromise study integrity or decrease safeguards for participants.
8. Decreasing the amount of blood draw or the frequency of blood draw
9. Reducing the time period of the study
10. Adjusting incentives (as long as they are not coercive or pose undue influence)

11. Response to a conditional approval determination by the convened IRB.

    [DHHS 45 CFR 46.110; FDA 21 CFR 56.110(b)]

3.4.2 Categories of Research Eligible for Expedited Review

Inclusion on this list merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects unless the reviewer determines otherwise for a study. The activities listed below should not be deemed to be of minimal risk simply because they are included on this list.

The expedited review procedure may not be used for the following:

- Where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal risk.

The availability of expedited review contained in paragraphs one (1) through nine (9) of this section below apply regardless of the age of subjects, unless specifically excepted as noted.

The standard requirements for informed consent (or its waiver, alteration, or exception) apply regardless of the type of review (i.e., expedited review or convened IRB review) used by the IRB. However, it should be noted that, while research that involves paragraphs one (1) through seven (7) below pertains to both initial review and continuing review, paragraphs eight (8) and nine (9) below only pertain to continuing reviews.

1. Clinical studies of drugs and medical devices only when condition (a) or (b) is met.
   a. Research on drugs for which an IND [21 CFR Part 312] is not required. (NOTE: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the produce is not eligible for expedited review.)
   b. Research on medical devices for which (i) an IDE [21 CFR Part 812] is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collections of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:

a. From healthy, non-pregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8-week period and collection may not occur more frequently than 2 times per week; or
b. From other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8-week period and collection may not occur more frequently than 2 times per week.

3. Prospective collection of biological specimens for research purposes by noninvasive means. Examples:
   a. Hair and nail clippings in a non-disfiguring manner.
   b. Deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction.
   c. Permanent teeth if routine patient care indicates a need for extraction.
   d. Excreta and external secretions (including sweat).
   e. Uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gum base or wax or by applying a dilute citric solution to the tongue.
   f. Placenta removed at delivery.
   g. Amniotic fluid obtained at the time of rupture of the membrane prior to or during labor.
   h. Supra-and sub-gingival dental plaque and calculus provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques.
   i. Mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings.
   j. Sputum collected after saline mist nebulization.

4. Collection of data through non-invasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where Medical Devices are employed, they must be cleared/approved for marketing.

   (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples:
   a. Physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject’s privacy.

b. Weighing or testing sensory acuity.
c. Magnetic resonance imaging.
d. Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography.
e. Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis).

   [NOTE: Some research in this category may be exempt from the DHHS regulations for the protection of human subjects. See exempt categories and 454 CFR 46.101(b)(4). This listing refers only to research that is not exempt.]

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

   [NOTE: Some Research in this category may be exempt from the DHHS regulations for the protection of human subjects. See exempt categories and 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.]

8. Continuing review of research previously approved by the convened IRB as follows:
   a. Where
      i. The research is permanently closed to the enrollment of new subjects.
      ii. All subjects have completed all research-related interventions; and
      iii. The research remains active only for long-term follow-up of subjects; or
   b. Where no subjects have been enrolled and no additional risks have been identified; or
   c. Where the remaining research activities are limited to data analysis.

Of note, category (8) identifies three situations in which research that is greater than minimal risk and has been initially reviewed by a convened IRB may undergo subsequent continuing review by the expedited review procedures.

For a multi-center protocol, an expedited review procedure may be used by the IRB at a particular site whenever the conditions of category (9) (a), (b), or (c) are satisfied for that site. However, with respect to category 9(b), while the criterion that "no subjects have been enrolled" is interpreted to mean that no subjects have ever been enrolled at a particular site, the criterion that "no additional risks have been identified" is interpreted to mean that neither the Investigator nor the IRB at a particular site has identified any additional risks from any site or other relevant source.

9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply by the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

   Under category (9), an expedited review procedure may be used for continuing review of research not conducted under an investigational new drug application or investigational device exemption where categories (2) through (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

Research in any of these categories may require review at a convened meeting of the IRB if the circumstances of the proposed research involve more than minimal risk. The expedited review procedure may not be used where identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that the risk related to invasion of privacy and breach of confidentiality is no greater than minimal. In addition, the expedited review procedures may not be used for classified research involving human subjects. Classified research is research that has a security classification established by an authorized agency of the federal government.

When the IRB is not required to conduct continuing review (for studies approved under the new common rule), records must provide a rationale for any decisions to conduct done continuing review of research otherwise eligible for review using the expedited procedure.

The IRB Chair or designee is responsible for reviewing and determining whether the research is eligible for review using the expedited review procedure. Reviewers use the reviewer checklist that includes the applicability of expedited review and the categories of research eligible for expedited review published in the Federal Register at 63 FR 60364-60367 to document that:

- The research is applicable for expedited review.
- The research is minimal risk.
- The research activities fall within one or more of the research categories eligible for expedited review; and
- The consent form includes the basic elements of informed consent or a waiver or alteration of informed consent is approved. If the proposed research is not eligible for review using the expedited review procedure, the reviewer requests the research activity be scheduled for full board review at a convened meeting of the IRB.
- The Chair or designee may approve, require modifications in (to secure approval), or defer action pending receipt of additional information from the Principal Investigator. The Chair or designee may not disapprove a research activity using the expedited review procedure; a research activity can only be disapproved by the IRB at a convened meeting.

3.4.3 Submission Requirements

A. When submitting applications for initial or continuing review using the expedited procedure, investigators must submit all applicable materials: protocol, consent, assent, and any other protocol related documents.

B. When submitting amendment requests for expedited review, investigators must submit all applicable materials (revised tracked and clean copies of modified documents) listed in HRPP policy [IRB Submission and Pre-Review].

C. Upon receipt of an application for expedited review, an IRB staff member pre-reviews the submission (e.g., to verify whether the materials are complete, required education has been completed, etc.) and makes an initial determination as to whether the submission is eligible for expedited review.

D. Continuing review of the research is required until the research has been completed or has been closed prior to completion. The investigator must submit the continuing review form in IRBManager to document that the study has been completed or is being closed prior to completion. For multi-site research, the research may be considered completed or may be closed prior to completion

when the investigator at this site is no longer collecting, receiving, or analyzing identifiable data.

E. During the trial the investigator should provide to the IRB all documents subject to review.

3.4.4 Expedited Review Procedures

Under an expedited review procedure, the review may be carried out by the IRB Chair designee. IRB members who serve as designees to the IRB Chair for expedited review will be matched as closely as possible with their field of expertise to the study under review. Only experienced IRB members may conduct reviews using the expedited procedure.

IRB members with a COI in the research (see IRB Member Conflict of Interest section in Policy 2) will not be selected to serve as expedited reviewers.

When reviewing research under an expedited review procedure, the IRB Chair, or designated IRB member(s), should receive and review all documentation that would normally be submitted for convened IRB review including the complete protocol. This includes review of the following:

1. The complete protocol or any protocol related documents
2. For continuing review, an application for continuing review that summarizes research activities since the previous annual review (including modifications and adverse events).
3. Notes from pre-screening conducted by the IRB staff.
4. Any applicable IRB applications.
5. The current consent document.
6. The investigator's current curriculum vitae, biosketch or other documentation evidencing qualifications.
7. Any newly proposed consent document.
8. Recruitment materials; and

9. A status report on the progress of the research including the following:

    a. number of participants accrued.

    b. a summary since the last IRB review of the following:

        i. unanticipated problems involving risks to participants or others.

        ii. participant withdrawals and the reasons for withdrawals.

        iii. complaints about the research.

        iv. any relevant recent literature.

        v. any interim findings.

        vi. any relevant multi-center trial reports.

        vii. the researcher's current risk-potential benefit assessment based on study results.

Protocols submitted for expedited review will be pre-screened by IRB staff to ensure that the package is complete. The reviewer(s) conducting initial continuing reviews or modifications to previously approved research will determine whether the research meets the criteria allowing review using the expedited procedure, and if so, whether the research meets the regulatory criteria for approval. If the research does not meet the criteria for expedited review, then the reviewer will indicate that the research requires convened IRB review, and the protocol will be placed on the agenda for the next IRB meeting.

In reviewing the research, the reviewers will follow the review procedures described in sections 3.7 and 3.8 and may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the convened IRB review procedure set forth below.

The IRB Chair (or designee) will indicate approval, required modifications or referral to the convened IRB. If modifications are required, the IRB staff will inform the Investigator. If the modifications are minor, the IRB Chair may determine if the Investigator has sufficiently addressed the modifications.

If research involving an FDA-regulated article is involved, a licensed physician must be involved in the review, unless the expedited submission is an administrative change and does not alter the risk/benefit ratio. See section 3.4.1 for examples of expedited

review that do not alter the risk/benefit ratio. The physician may be a voting IRB member or a consultant.

Research for which limited IRB review is a condition of exemption under §46.104(d)(2)(iii) and (d)(3)(i)(C) is permitted through an expedited review process.

Regulations & Guidance: DHHS 45 CFR 46.100; FDA 21 CFR 46.110; Categories of Research that May Be Reviewed by the IRB through an Expedited Review Procedure - FDA & DHHS; OHRP Guidance on Written IRB Procedures and 45CFR 46.108(a)(3) and (4); OHRP Guidance on Use of Expedited Review Procedures; OHRP Guidance on Continuing Review; FDA Information Sheets: Continuing Review after Study Approval

3.4.5 Informing the IRB

All members of the IRB will be apprised of all expedited review approvals that were reviewed by the IRB Chair (or designee). This notification is accomplished by means of a list in the agenda and/or a list in the monthly IRB meeting minutes. Any IRB member can request to review the full expedited review and all supporting documentation by contacting the IRB office.

3.5 Convened IRB Review

Convened IRB review means review by a fully convened IRB. Except when an expedited review procedure is used, the IRB will conduct initial, continuing reviews and modifications of previously approved research at convened meetings at which a quorum (see section 3.5.6) of the members is present. Regulations and Guidance: FDA 21 CFR 56.108(c)

3.5.1 IRB Meeting Schedule

The IRB meets on a regular basis throughout the year. The schedule for the IRB may vary due to holidays or lack of quorum. The schedule for IRB meetings is given to all IRB members in December before the next calendar year. Additionally, this information is posted on the Pennington Biomedical Research Center HRPP website for the benefit of all Investigators, research coordinators and other research staff when submitting protocol materials. Special meetings may be called at any time by the IRB Chair.

3.5.2 Preliminary Review

The IRB staff will perform a preliminary review of all submission materials submitted for determination of completeness and accuracy. Only complete submissions will be referred for further consideration (i.e., exempt, expedited or convened IRB review).

The IRB obtains a copy of the following documents, if applicable: the protocol, the amendment, written informed consent form(s) and consent form updates that the investigator proposes for use in the trial, subject recruitment procedures (e.g. advertisements), written information to be provided to subjects, Investigators Brochure (IB), available safety information, information about payments and compensation available to subjects, the investigator's current curriculum vitae and/or other documentation evidencing qualifications, and any other documents that the IRB may need to fulfill its responsibilities. The IRB considers the qualifications of the investigator for the proposed trial, as documented by a current curriculum vitae and/or by any other relevant documentation the IRB requests.

The Investigator will be informed either by IRBManager, e-mail or phone of missing materials and the deadline to resubmit corrections before further review can take place.

3.5.3 Primary Reviewers

After it has been determined that the protocol submission is complete, the IRB Chair, with the assistance of the IRB Staff, assigns protocols for review based on the scientific content of the protocol, reviewer's area of expertise, requirements for representation of vulnerable populations involved in the research, and study procedures described in the protocol and the experience and expertise of the members attending the meeting. The qualifications, experience, and expertise, as well as representative capacity of each member are documented in the IRB roster. A primary reviewer is assigned to each agenda item and a scientific/scholarly reviewer to each agenda item who has expertise in the area of research (one person could do both).

When the IRB is presented with a protocol which, may be outside of the knowledge base or representative capacity of all of the IRB members, an outside consultant will be sought (see sections 3.6.6, Consultant - Children and section 3.6.7, Consultant - Vulnerable Populations). Proposals for which appropriate expertise cannot be obtained for a given meeting will be deferred to another meeting when appropriate expertise can be achieved.

Primary reviewers are responsible for:

- Having a thorough knowledge of all details of the proposed research.
- Performing an in-depth review of the proposed research and supporting documents.
- Leading the discussion of the proposed research at the convened meeting and presenting both positive and negative aspects of the research. (section 3.6.4 – Initial, Continuing Review and Requests for Modification).
- Making suggestions for changes to the proposed research.
- Completing all applicable IRB Member Reviewer Forms.

If the primary reviewer will be absent from the meeting, a new reviewer with appropriate expertise will be assigned if time allows. If the reviewer is unable to attend the meeting and an alternate is not able to be assigned, the submission will be tabled until the appropriate expertise can be obtained.

It should be noted that all IRB members have access to and are expected to review all IRB proposals, not just the ones they are responsible for reviewing.

During the convened IRB meeting, primary reviewers must give the IRB staff the completed and appropriate reviewer forms. All reviewer forms will be filed with the appropriate meeting.

3.5.4 Pre-Meeting Distribution of Documents to Reviewers

Documents reviewed by expedited review are not submitted to members.

The following materials will be distributed to primary reviewers:

- Initial submissions – Application for Initial Review (submitted by investigator), any relevant appendices, any relevant grant applications; the protocol; sponsor or DHHS approved protocol (if one exists), the DHHS approved sample consent (if one exists), the Investigator's Brochure (when one exists); the sample informed consent document (when one exists); the complete consent document , recruitment materials (if available), any supporting documents and any other protocol related documents (including, if applicable, a summary of findings from nonclinical studies that potentially have clinical significance and from clinical trials that are relevant to the trial.)
- Continuing review submissions - the primary reviewer will receive the following:
    - the continuing review report,
    - the last approved consent,
    - the complete protocol, protocol summary or application containing the relevant information necessary to determine whether the proposed

research continues to fulfill the criteria for approval. Investigator brochure (if one exists), all protocol modifications reviewed during the current continuing review timeframe, all adverse events reviewed during the current continuing review timeframe, all protocol deviations reviewed during the current continuing review time frame.

- Modifications – the primary reviewer will receive a copy of all items being modified, and an application for a modification of approved human research.

The following materials will be distributed to all attending members not involved in the primary review:

- Initial submissions – all members will receive the Initial Submission Application, protocol summary or protocol, the complete consent document, recruitment materials (if available) and any supporting documentation. All members have access to all documents via IRBManager.
- Continuing review submissions – all members will receive the continuing review submission form (which includes a status report), the full protocol, or a protocol summary containing the relevant information necessary to determine whether the proposed research continues to fulfill the criteria for approval, and the most recently approved consent document. All members have access to all documents via IRBManager.
- Modifications – all members will receive the modification submission form; a copy of items being modified or a summary of the modifications containing the relevant information necessary to determine whether the modification meets the criteria for approval. All members have access to all documents via IRBManager.

Documents are distributed to IRB members approximately one week before the IRB meeting to allow adequate review time.

3.5.5 IRB Agenda

While the IRB will make every effort to review all submissions, the IRB has the right to limit the agenda based on IRB member attendance of appropriate expertise.

3.5.6 Quorum

Human subjects research and clinical investigations that cannot be reviewed using the expedited review procedure are reviewed at a convened meeting of the IRB at which a quorum has been confirmed. A quorum consists of a simple majority (more than fifty percent (50%) of the voting IRB membership, including at least one member whose primary concern is in a non-scientific area, and one unaffiliated. For research to be

approved it has to receive the approval of a majority of members present at the meeting. If a regular IRB member and his/her alternate are present at a convened IRB meeting, only one counts towards the quorum and the IRB member (not the alternate) is the only one entitled to vote.

Additional quorum requirements include the following:

- If research involving an FDA-regulated article is involved, a licensed physician must be involved in the review. The physician may be a voting IRB member or a consultant. The review can be provided via email, fax, mail or the reviewer may be present for the discussion and for the review of any studies (including initial review, continuing review, modification, investigator's brochure or report of unanticipated problems involving risks to subjects and others) that involve the FDA-regulated article; and
- For research that involves, individuals with impaired decision-making capacity, IRB membership must include at least one member who is an expert in the area of the research.

At meetings of the IRB, a quorum must be established and maintained for the deliberation and vote on all matters requiring a vote. The IRB Chair, with the assistance of the IRB staff, will confirm that an appropriate quorum is present before calling the meeting to order. If an IRB member leaves the meeting due to a conflict of interest or any other reason the IRB Chair and/or IRB staff are responsible for assuring a quorum is maintained. The IRB staff will document in the meeting minutes the quorum determination. If a quorum is not maintained, the proposal or pending action item must be tabled, or the meeting terminated. The IRB staff will document the arrival and departure for all IRB members and notify the IRB Chair if a quorum is not present. The IRB staff documents attendance of IRB members, guests and ex-officio (non-voting members) guests.

IRB members are considered present and participating at a duly convened IRB meeting when either physically present or participating through electronic means (e.g., teleconferencing or video conferencing) that permits them to listen to and speak during IRB deliberations and voting.

When not physically present, the IRB member must have received all pertinent materials prior to the meeting and must be able to participate actively and equally in all discussions.

Opinions of absent IRB members that are transmitted by mail, voicemail, facsimile or e-mail may be considered by the attending IRB members, but may not be counted as votes or to satisfy the quorum for convened meetings.

IRB members who have an alternate member should contact the IRB office by e-mail or phone approximately two weeks before a scheduled IRB meeting date if unable to make the IRB meeting so IRB staff can ensure appropriate notification of IRB alternate members.

3.6 IRB Meeting Procedures

3.6.1 Call to Order and Quorum

The IRB Chair (or designee in the event that the IRB Chair is absent) will call the IRB meeting to order, once it has been determined that a quorum exists.

3.6.2 Conflict of Interest of IRB Members

Where there is a conflict of interest involving an IRB member, the IRB Chair (or designee) will remind the IRB member to recuse him/herself from the discussion and vote by leaving the room when there is a conflict for the particular action item under review. If the IRB member is a member of the research team, the member may provide additional information if requested by the board but exits the room before final discussion and vote. Known conflicts of interest of an IRB member are also noted on the agenda, which is made available to all members prior to the IRB meeting.

3.6.3 Review and Approval of Prior Meeting Minutes

The IRB will review and discuss the IRB meeting minutes from the previous meeting and determine if there are any revisions/corrections to be made. If there are no changes to be made, the minutes will be accepted as presented and considered final. If it is determined that revisions/corrections are necessary, the Chair will conditionally approve the minutes and approve the final version with the requested changes. A majority of the members present at a duly constituted IRB meeting are required to accept the minutes.

3.6.4 Initial, Continuing Review and Requests for Modification

The IRB reviews all submissions for initial review and continuing review, as well as requests for modifications. If a primary reviewer is unable to attend the meeting and an alternate with the appropriate expertise is not available, the item will be tabled until the next meeting. All IRB members present at a duly convened IRB meeting have full voting rights, except in the case of a conflict of interest (see IRB Member Conflict of Interest section in Policy 2), ex-officio members, and alternate members present at the same meeting which the regular member for which they alternate is also present (see section 3.5.6 – Quorum). In order for the research to be approved, it must receive the

approval of a majority of those voting members present at a duly constituted IRB meeting.

The primary reviewer presents a brief synopsis of the research protocol, with the expectation that the other members have reviewed the protocol materials. The primary reviewer is responsible for covering the scientific background and rationale, study design, how the research differs from and compares to standard care, appropriateness of the study population and the inclusion/exclusion criteria, the risks and potential benefits to subjects, alternative treatments or procedures, as well as the criteria for IRB approval and, when applicable, additional protections for pregnant women, human fetuses, and neonates; children; and individuals with impaired decision-making capacity.

Secondary reviewers are asked to present any additional clarifications or commentary on the study plan, and any questions or concerns, or modifications he/she would require for approval.

Both the primary and secondary reviewers are expected to provide an in-depth review of the consent form and identify missing required elements and when, applicable, additional elements for informed consent. Additionally, reviewers may comment on the reading level and style of the consent form and provide detailed suggestions for improvement. Consent form comments may be handwritten on the form or provided in written commentary as part of the review.

When applicable, both the primary and secondary reviewers are responsible for reviewing the investigational drug brochure or investigational device information, or NIH or other federal grant application or proposal for funding.

Reviewers are encouraged, although not required, to contact the principal investigator prior to the meeting if they have questions about the study, particularly if they have significant concerns about the study or believe additional information is needed for the IRB to be able to assess the risks and anticipated benefits, if any, to subjects and the importance of the knowledge that may be expected to result from the research.

Reviewers are encouraged to provide written comments to ensure that the IRB staff convey the modifications required and/or questions and concerns raised by the IRB completely, accurately and precisely. After the primary and secondary reviewers have presented the study and their review comments, the Chair opens the protocol up for discussion by the membership. The Chair and members may direct specific questions to the assigned reviewers or to other members with specific expertise or viewpoints. Only members who participate in the IRB review and discussion are allowed to vote.

At the end of the discussion, one of the reviewers or another member makes a motion to approve, require modifications in the research (to secure approval), defer action on (pending receipt of additional information), or disapprove the protocol. The IRB may request more information be given to subjects when, in the judgement of the IRB, the additional information would add meaningfully to the protection of the rights, safety and/or well-being of the subjects. A vote on the motion is taken (for, against, or abstain) by show of hands or voice vote and recorded in the Minutes. All motions are decided by majority vote of the members present for the review. A quorum of the members of the IRB (more than one-half the members) must be present in order for the IRB to take a vote.

Regulations & Guidance: DHHS 45 CFR 46.103(b) (4); 45 CFR 46.108(b); 45 CFR 46.109; 45 CFR 46.116(b) (5); FDA 21 CFR 50.25(b) (5); 21 CFR 56.108; OHRP Guidance on Written IRB Procedures and 45CFR 46.108(a)(3) and (4); OHRP Guidance on Continuing Review; FDA Information Sheets: Continuing Review after Study Approval

3.6.5 Recording of Proceedings

It is the responsibility of the IRB staff to record the proceedings of the IRB meeting with digital equipment to ensure accuracy of discussion. All recording of proceedings is destroyed upon approval of the minutes. In addition, the IRB staff is responsible for taking minutes at each IRB meeting.

In order for research activity to be approved, it must receive the approval of a majority of those members present at a convened IRB meeting. The vote is recorded by means of signifying for, against, and abstained by show of hands. The vote is recorded by the staff and reflected on the IRB meeting minutes.

3.6.6 Consultant - Children

When reviewing a protocol involving children, the IRB will ensure that appropriate pediatric expertise is available to review the specific research activities. Non-voting consultants may be invited to assist with the review if additional expertise is needed.

3.6.7 Consultant - Vulnerable Populations

When reviewing studies with other vulnerable populations, including pregnant women, fetuses, neonates, handicapped persons, and individuals with impaired decision-making capacity, the IRB will request review by an expert consultant, as needed. If the IRB regularly reviews research involving a vulnerable category of subjects, one or more individuals who are knowledgeable about and experienced in working with these

subjects should be included as IRB members (refer to policy on vulnerable subjects for more detail section 3.7.6 – Vulnerable Populations).

3.6.8 Guests and Non-Voting Members

At the discretion of the IRB, the Investigator (or designee such as a Co-Investigator) may be invited to the IRB meeting to answer questions about the proposed or ongoing research. The Investigator may not be present for the discussion or vote on the study or action under review by the IRB.

Potential new IRB members may be invited to attend IRB meetings as a guest at the discretion of the IRB Chair. Invited guests may not speak unless requested by the IRB and must sign a confidentiality agreement prior to the convened meeting.

Certain ex-officio individuals (non-voting members, IRB staff) regularly attend IRB meetings as ex-officio guests. While they are not voting members of the IRB, they may participate in the IRB discussion and may provide additional information to the IRB. The IRB Chair may ask the ex-officio individual to formally review an IRB submission if the ex-officio's expertise is warranted. However, the non-voting member will not be asked to be the primary reviewer as the non-voting member has no voting rights.

3.7 Criteria for IRB Approval of Research

At the time of initial, continuing review and review of a modification to previously approved research (if the modification affects the criteria for approval), the IRB must determine that the following requirements are satisfied to approve research involving human subjects.

Risks to subjects are minimized:

- By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk; and
- Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes.
- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result.
- In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research).

- The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
- Selection of subjects is equitable. In making this assessment, the IRB should consider the purpose of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, pregnant women, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.
- Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116 or 21 CFR 50.20.
- Informed consent will be appropriately documented, in accordance with, and to the extent required by 45 CFR 46.117 or 21 CFR 50.27.
- When appropriate, the research plan makes adequate provisions for monitoring the data collected to ensure the safety of subjects.
- When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
- When some or all the subjects are likely to be vulnerable to coercion or undue influence, such as children, pregnant women, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects.
- Research studies have the resources necessary to protect participants:
    - Adequate time for the researchers to conduct and complete the research.
    - Adequate number of qualified staff.
    - Adequate facilities.
    - Access to a population that will allow recruitment of the necessary number of participants.
    - Availability of medical or psychosocial resources that participants may need as a consequence of the research.

Regulations & Guidance: DHHS 45 CFR 46.111; FDA 21 CFR 56.111

3.7.1 Risk-Benefit Assessment

The goal of a risk-benefit assessment is to ensure that the risks to research subjects posed by participation in a research study are justified relative to the anticipated benefits for the subjects or society. The IRB must:

- Judge whether the anticipated benefit, either of new knowledge or of improved health for the research subjects, justifies asking any person to undertake the risks.
- Disapprove research in which the risks are judged unreasonable in relation to the anticipated benefits.

The assessment of the risks and benefits of the proposed research involves a series of steps:

- Identify the risks associated with the research, as distinguished from the risks of therapies the subjects would receive even if not participating in research.
- Determine whether the risks to subjects will be minimized to the extent possible. This can be done, for example by using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk. This also can be accomplished, as appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes; identify the probable benefits to be derived from the research; determine whether the risks to subjects are reasonable in relation to the benefits to subjects, if any, and assess the importance of the knowledge to be gained.
- In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research.
- The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g., the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.
- Ensure that potential subjects will be provided with an accurate and fair description of the risks or discomforts and the anticipated benefits.

Based on this assessment, risk associated with the research will be classified as either minimal risk or greater than minimal risk, which will be based on the interpretation of minimal risk.

Regulations & Guidance: DHHS 45 CFR 46.111(a); FDA 21 CFR 56.111(a)

3.7.1.1 Scientific Merit

In order to assess the risks and benefits of the proposed research, the IRB must determine that the research uses procedures consistent with sound research design, the research design is sound enough to reasonably expect the research to answer its proposed question and the knowledge expected to result from this research is sufficiently important to justify the risk.

The IRB considers the following during the initial protocol review:

- Does the protocol accurately describe the following in a clear, detailed method?
    - Objectives and the purpose of research

    - References to literature and data that are relevant to the trial, and that provide background for the research.

        - Setting of research
        - Procedures of research
        - Data and safety monitoring plan
        - Risks of research
        - Potential benefits of research
        - Alternatives to participation in research
        - The Investigator has demonstrated a potential for recruiting the required number of suitable subjects within the agreed recruitment period.
- Is the available non-clinical and clinical information on an investigational product adequate to support the proposed clinical trial?
- All research involving DXA and medical procedures under the purview of Pennington Biomedical Research Center must have a qualified physician, credentialed by Pennington Biomedical that will be responsible for all trial related medical decisions.

    Regulations & Guidance: DHHS 45 CFR 46.111(a) (1); FDA 21 CFR 56.111(a) (1), ICH GCP guidance E6

3.7.2 Equitable Selection of Subjects

The IRB determines by viewing the protocol that the selection of subjects is equitable with respect to gender, age, class, etc. The IRB will not approve a study that does not provide adequately for the equitable selection of subjects or has not provided an appropriate scientific and ethical justification for excluding classes of persons who might benefit from the research. In making this determination, the IRB evaluates:

- the purpose of the research.
- the setting in which the research occurs;
    - scientific and ethical justification for including vulnerable populations such as children, pregnant women, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.
- the scientific and ethical justification for excluding classes of persons who might benefit from the research.

- inclusion/exclusion criteria.
- payment amount and timing of payments to participants (see 3.8.9 – Payment to Research Subjects); and
- participant recruitment and enrollment procedures.

At the time of the continuing review, the IRB will determine if the Investigator has followed the subject selection criteria that he/she originally set forth at the time of initial IRB review and approval.

Regulations & Guidance: DHHS 45 CFR 46.111(a) (3); FDA 21 CFR 56.111(a) (3)

3.7.2.1 Recruitment of Subjects

The Investigator will provide the IRB with all recruiting materials to be used in identifying subjects including recruitment methods, advertisements, and payment arrangements. See Section 3.8.8 - Advertisements for a discussion of IRB review of advertisements, and section 3.8.9 - Payment to Research Subjects for a discussion of IRB review of payments/compensation to subjects.

Regulations & Guidance: DHHS 45 CFR 46.111(a) (3); 45 CFR 46.116; FDA 21 CFR 50.20; 21 CFR 56.111(a) (3)

3.7.3 Informed Consent

The IRB will determine the following:

- Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by 45 CFR 46.116 and 21 CFR 50.20.

In addition, the IRB will ensure that the consent will be appropriately documented according to legal requirements in accordance with, and to the extent required by 45 CFR 46.117 and 21 CFR 50.27 (see Policy 5 - Obtaining Informed Consent from Research Subjects for further information on Informed Consent elements).
Regulations & Guidance: DHHS 45 CFR 46.111(a) (4) & (a) (5); FDA 21 CFR 56.111(a) (4) & (a) (5).

3.7.4 Safety Monitoring

Pennington Biomedical Research Center requires that all research must have a data safety monitoring plan. Any reports generated from the data safety monitoring plan will be submitted to the IRB and forwarded to the Medical Staff for review.

The data safety monitoring plan must describe the procedures for safety monitoring, reporting of unanticipated problems involving risks to subjects or others, descriptions of interim safety reviews and the procedures planned for transmitting the results to the IRB. This description should include information regarding an independent Data and Safety Monitoring Board (DSMB), if one exists, or an explanation why an independent data safety monitor is not necessary.

The IRB determines that the data safety monitoring plan makes adequate provisions for monitoring the reactions of subjects and the collection of data to ensure the safety of subjects. The overall elements of the monitoring plan may vary depending on the potential risks, complexity, and nature of the research study. The method and degree of monitoring needed is related to the degree of risk involved. Monitoring may be conducted in various ways or by various individuals or groups, depending on the size and scope of the research effort. These exist on a continuum from monitoring by the Investigator in a small, low risk study to the establishment of an independent DSMB for a large phase III clinical trial.

The factors the IRB will consider in determining whether the safety monitoring plan is adequate for the research are as follows:

1. Monitoring is commensurate with the nature, complexity, size and risk involved.

2. Monitoring is timely. Frequency should be commensurate with risk. Conclusions are reported to the IRB.

3. For low-risk studies, continuous, close monitoring by the study Investigator or an independent individual may be an adequate and appropriate format for monitoring, with prompt reporting of problems to the IRB, sponsor and regulatory bodies as appropriate.

4. For an individual Safety Monitor, the plan must include:

    - parameters to be assessed,
    - methods and timing for assessing, including the mechanism to assess the critical efficacy endpoints at intervals in order to determine when to continue, modify, or stop a study.
    - frequency of monitoring procedures for reporting to the IRB
    - recording of safety parameters

5. For a DSMB, the plan must include:

    - name of the Data Safety Monitoring Board, if applicable,

- is independent from the sponsor,
- availability of written reports,
- composition of the monitoring group (if a group is to be used),
- experts in all scientific disciplines needed to interpret the data and ensure patient safety. Clinical trial experts, biostatisticians, bioethicists, and clinicians knowledgeable about the disease and treatment under study should be part of the monitoring group or be available if warranted,
- frequency and content of meeting reports,
- frequency and character of monitoring meetings (e.g., open or closed, public or private).

In general, it is desirable for a DSMB to be established by the study sponsor for research that is blinded, involves multiple sites, involves vulnerable subjects, or employs high-risk interventions. The IRB has the authority to require a DSMB as a condition for approval of research where it determines that such monitoring is needed. When DSMBs are utilized, IRBs conducting continuing review of research may rely on a current statement from the DSMB indicating that it has and will continue to review study-wide adverse events, interim findings, and any recent literature that may be relevant to the research, in lieu of requiring that this information be submitted directly to the IRB.

Regulations & Guidance: DHHS 45 CFR 46.111(a) (6); FDA 21 CFR 56.111(a) (6), CFR 46.108(a)(3)(iii)

3.7.5 Privacy and Confidentiality

Under the research regulations, the IRB is required to determine whether adequate procedures are in place to protect the privacy of subjects and to maintain the confidentiality of the data.

3.7.5.1 Definitions

Confidentiality: methods used to ensure that information obtained by researchers about their research subjects is not improperly divulged.

Identifiable Information: for research privacy purposes, this means information where the identity of the subject is or may readily be ascertained by the Investigator or associated with the information.

Individually Identifiable Private Information: is information where, for research purposes, the identity of the subject is or may readily be ascertained by the Investigator or associated with the information.

Obtain: means to receive or access Individually Identifiable Private Information (or identifiable specimens) for research purposes. This includes an Investigator's use, study, or analysis for research purposes of Individually Identifiable private Information (or identifiable specimens) already in the possession of the Investigator.

Private information: for research privacy purposes, this means information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (e.g., a medical record). [45 CFR 46.102(f)]

3.7.5.2 Privacy

The IRB must determine whether the activities in the research constitute an invasion of privacy. In order to make that determination, the IRB must obtain information regarding how the Investigators are getting access to subjects or subjects' private, identifiable information. Investigators must have an appropriate authorization to access subjects or the subjects' information.

In developing strategies for the protection of subjects' privacy, consideration should be given to:

- Methods used to identify and contact potential subjects.
- Settings in which an individual will be interacting with an Investigator.
- Appropriateness of all personnel present for research activities.
- Methods used to obtain information about subjects and the nature of the requested information.
- Information that is obtained about individuals other than the target subjects, and whether such individuals meet the regulatory definition of human subject (e.g., a subject provides information about a family member for a survey); and
- How to access the minimum amount of information necessary to complete the study.

3.7.5.3 Confidentiality

The level of confidentiality protections should be commensurate with the potential of harm from inappropriate disclosure.

At the time of initial review, the IRB ensures that the privacy and confidentiality of research subjects are protected. The IRB assesses whether there are adequate

provisions to protect subject privacy and maintain confidentiality. The IRB does this through the evaluation of the methods used to obtain information:

- About subjects.
- About individuals who may be recruited to participate in studies.
- The use of personally identifiable records; and
- The methods to protect the confidentiality of research data.

The Investigator will provide information regarding the privacy and confidentiality of research subjects at the time of initial review through the completion of the study; Pennington Biomedical Research Center approved HIPAA Authorization Form, and/or other submitted, applicable materials. The IRB will review all information received from the Investigator and determine whether or not the privacy and confidentiality of research subjects is sufficiently protected. In some cases, the IRB may also require that a certificate of confidentiality be obtained to additionally protect research data from compulsory disclosure.

Certificates of Confidentiality are issued by the National Institutes of Health (NIH) and other HHS agencies to protect identifiable research information from forced or compelled disclosure. The requirements for obtaining a certificate of confidentiality are as follows:

- Research is automatically covered by a certificate of confidentiality whenever the study is funded in whole or in part by the NIH and involves identifiable, sensitive information.
- The term “identifiable sensitive information” means information is considered "sensitive" if the loss of confidentiality, integrity, or availability could be expected to have a serious, severe or catastrophic adverse effect on organizational operations, organizational assets, or individuals. Personally identifiable data is sensitive if disclosure of such data would pose increased social/reputational, legal, employability, or insurability risk to subjects. For the purposes of the Policy, consistent with subsection 301(d) of the Public Health Service Act (42 U.S.C 241), the term “identifiable, sensitive information” means information about an individual that is gathered or used during biomedical, behavioral, clinical, or other research, where the following may occur:
    - An individual is identified; or
    - For which there is at least a very small risk, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.

- Examples of research automatically covered by a certificate of confidentiality include:
    - Biomedical, behavioral, clinical, or other research, including exempt research, except where the information obtained is recorded in such a manner that human participants cannot be identified or the identity of the human participants cannot readily be ascertained, directly or through identifiers linked to the participants.
    - The collection or use of biospecimens that are identifiable to an individual or for which there is at least a very small risk that some combination of the biospecimen, a request for the biospecimen, and other available data sources could be used to deduce the identity of an individual.
    - The generation of individual level, human genomic data from biospecimens, or the use of such data, regardless of whether the data is recorded in such a manner that human participants can be identified, or the identity of the human participants can readily be ascertained.
    - Any other research that involves information about an individual for which there is at least a very small risk, as determined by current scientific practices or statistical methods, that some combination of the information, a request for the information, and other available data sources could be used to deduce the identity of an individual.
- Researchers may also apply for a certificate of confidentiality for non-federally funded research.
- When research is covered by a certificate of confidentiality, researchers:
    - May not disclose or provide, in any federal, state, or local civil, criminal, administrative, legislative, or other proceeding, the name of such individual or any such information, document, or biospecimen that contains identifiable, sensitive information about the individual and that was created or compiled for purposes of the research, unless such disclosure or use is made with the consent of the individual to whom the information, document, or biospecimen pertains; or
    - May not disclose or provide to any other person not connected with the research the name of such an individual or any information, document, or biospecimen that contains identifiable, sensitive information about such an individual and that was created or compiled for purposes of the research.
    - May disclose information only when:

- Required by federal, state, or local laws (e.g., as required by the Federal Food, Drug, and Cosmetic Act, or state laws requiring the reporting of communicable diseases to state and local health departments), excluding instances of disclosure in any federal, state, or local civil, criminal, administrative, legislative, or other proceeding.
- Necessary for the medical treatment of the individual to whom the information, document, or biospecimen pertains and made with the consent of such individual.
- Made with the consent of the individual to whom the information, document, or biospecimen pertains; or
- Made for the purposes of other scientific research that is in compliance with applicable federal regulations governing the protection of human subjects in research.

- When research is covered by a certificate of confidentiality, researchers must inform participants (for example, in the consent document) of the protections and limitations of certificates of confidentiality:
  - For studies that were previously issued a Certificate, and participants were notified of the protections provided by that Certificate, NIH does not expect participants to be notified that the protections afforded by the Certificate have changed, although IRBs may determine whether it is appropriate to inform participants.
  - If part of the study cohort was recruited prior to issuance of the Certificate, but are no longer actively participating in the study, NIH does not expect participants consented prior to the change in authority, or prior to the issuance of a Certificate, to be notified that the protections afforded by the Certificate have changed, or that participants who were previously consented to be re-contacted to be informed of the Certificate, although IRBs may determine whether it is appropriate to inform participants.
- Researchers conducting NIH-supported research covered by a certificate of confidentiality must ensure that if identifiable, sensitive information is provided to other researchers or organizations, regardless of whether or not the research is federally funded, the other researcher or organization must comply with applicable requirements when research is covered by a certificate of confidentiality.

- Researchers conducting research covered by a certificate of confidentiality, even if the research is not federally funded, must ensure that if identifiable, sensitive information is provided to other researchers or organizations, the other researcher or organization must comply with applicable requirements when research is covered by a certificate of confidentiality.

In reviewing confidentiality protections, the IRB shall consider the nature, probability, and magnitude of harm that would be likely to result from a disclosure of collected information outside the research. It shall evaluate the effectiveness of proposed de-identification techniques, coding systems, encryption methods, storage facilities, access limitations, and other relevant factors in determining the adequacy of confidentiality protections.

Regulations & Guidance: DHHS 45 CFR 46.111(a) (7); FDA 21 CFR 56.111(a) (7)

3.7.6 Vulnerable Populations

At the time of initial review, the IRB will consider the scientific and ethical reasons for including vulnerable subjects in research. The IRB may determine and require, when appropriate, additional safeguards put into place for vulnerable subjects, such as those without decision-making capacity.

For an extensive discussion about the IRB's review and approval process for individual populations of vulnerable subjects, please refer to Policy 6 - Vulnerable Subjects in Research.

Regulations & Guidance: DHHS 45 CFR 46.111(b); 45 CFR 46 Subpart B, Subpart C & Subpart D; 45 CFR 46.205; FDA 21 CFR 50.3; 21 CFR 56.111(b)-(c); 21 CFR Subpart D

3.8 Additional Considerations during IRB Review and Approval of Research

3.8.1 Determination of Risk

At the time of initial review and continuing review, the IRB will make a determination regarding the risks associated with the research proposals. Risks associated with the research will be classified as either minimal risk or greater than minimum risk based on the absolute interpretation of minimal risk. The meeting minutes will reflect the IRB's determination regarding risk levels.

3.8.2 Frequency of Review

At the time of initial review and at continuing review, the IRB will make a determination regarding the frequency of review of the research protocols. All protocols will be reviewed by the IRB at intervals appropriate to the degree of risk but no less than once per year. In some circumstances, a shorter review interval (e.g., semi-annually, quarterly, or after accrual of a specific number of subjects) may be required (see section 3.8.3 - Review More Often than Annually). The meeting minutes will reflect the IRB's determination regarding review frequency.

3.8.2.1 Exempt and Expedited

For studies approved after January 21, 2019 under the exempt and expedited review categories, a status report is required.

For expedited studies, a status report is required every three years.

For exempt studies, a status report must be received every five years. Modifications are submitted in cases when the change alters the risk, the scope of the project, or falls under a limited review category.

3.8.2.1 Full Board

For full Board studies approved after January 21, 2019, continuing review is required annually, except in the following circumstance:

- The research that is not FDA regulated, interventions have concluded, and the study is only:
- Analyzing data, including identifiable private information or identifiable biospecimens, and
- Accessing follow-up clinical data from clinical care procedures.

A status report is required every three years for these studies.

Regulations & Guidance: DHHS 45 CFR 46.109(e); FDA 21 CFR 56.109(f); CFR 115

3.8.3 Review More Often Than Annually

Unless specifically waived by the IRB, research that meets any of the following criteria will require review more often than annually:

- Significant risk, as determined by the IRB, to research subjects (e.g., death, permanent or long-lasting disability or morbidity, severe toxicity) without the possibility of direct benefit to the subjects.
- The involvement of especially vulnerable populations likely to be subject to coercion (e.g., terminally ill); or
- A history of serious or continuing non-compliance on the part of the Investigator.

The following factors also will be considered when determining which studies require review more frequently than on an annual basis:

- The probability and magnitude of anticipated risks to subjects.
- The likely medical condition of the proposed subjects.
- The overall qualifications of the Investigator and other members of the research team.
- The specific experience of the Investigator and other members of the research team in conducting similar research.
- The nature and frequency of adverse events observed in similar research at this and other Institutions.
- The novelty of the research making unanticipated adverse events more likely; or
- Any other factors that the IRB deems relevant.

In specifying an IRB approval period of less than one year, the IRB may define the period with either a time interval or a maximum number of subjects either studied or enrolled. If a maximum number of subjects studied or enrolled is used to define the approval period, it is understood that the approval period in no case can exceed one year and that the number of subjects studied or enrolled determines the approval period only when that number of subjects is studied or enrolled in less than one year.

If an approval period of less than one year is specified by the IRB, the reason for more frequent review must be documented in the minutes.

3.8.4 Independent Verification That No Material Changes Have Occurred

The IRB recognizes that protecting the rights and welfare of subjects sometimes requires that the IRB independently verify utilizing sources other than the Investigator that no material changes occurred during the IRB designated approval period. Independent verification from sources other than the Investigator may be necessary at times (e.g., in cooperative studies, or other multi-center research).

The IRB will determine the need for verification from outside sources on a case-by-case basis and according to the following criteria:

- Protocols where concern about possible material changes occurred without IRB approval have been raised based on information provided in continuing review reports or from other sources.
- Protocols conducted by Investigators who have previously failed to comply with federal regulations and/or the requirements or determinations of the IRB.
- Protocols randomly selected or for cause audits conducted internally; or
- Whenever else the IRB deems verification from outside sources is relevant.

The following factors also will be considered when determining which studies require independent verification:

- The probability and magnitude of anticipated risks to subjects.
- The likely medical condition of the proposed subjects; or
- The probable nature and frequency of changes that may ordinarily be expected in the type of research proposed.

The IRB must determine which clinical investigations need verification from sources other than the clinical investigator that no material changes in the research have occurred since the previous IRB review. The IRB should consider:

- The vulnerability of the participants.
- The projected rate of enrollment.
- Whether the study involves novel therapies.

In making determinations about independent verification, the IRB may prospectively require that such verification take place at predetermined intervals during the approval period or may retrospectively require such verification at the time of continuing review, review of amendments and/or unanticipated problems.

If any material changes have occurred without IRB review and approval, the IRB will decide the corrective action to be taken. (See Policy 10 - Non-Compliance)

3.8.5 Consent Monitoring

In reviewing the adequacy of subject informed consent procedures for proposed research, the IRB may on occasion determine that special monitoring of the consent process by an impartial observer (i.e., a consent monitor) is required to reduce the possibility of coercion and undue influence.

Such monitoring may be particularly warranted when the research presents significant risks to subjects, or if subjects are likely to have difficulty understanding the information that will be provided. Monitoring may also be appropriate as a corrective

action where the IRB has identified problems associated with a particular Investigator or a research project.

Regulations & Guidance: DHHS 45 CFR 46.109(e); FDA 21 CFR 56.109(f)

3.8.6 Investigator Conflicts of Interest

The research application asks protocol-specific questions regarding conflict of interests for Investigators and key research personnel. As part of its review process, the IRB notifies the Director of Legal and Regulatory Compliance of the potential conflict. (See Policy 401.00 – Individual Financial Conflict of Interest).

Regulations & Guidance: 42 CFR 50.603; 42 CFR 50.606(a); FDA 21 CFR 50.606(a): 21 CFR 54.1; 21 CFR 54.2; 21 CFR 54.4; 21 CFR 312.64(d); 21 CFR 812.110(d); 45 CFR 690

3.8.7 Significant New Findings

During the course of research, significant new knowledge or findings about the medication and/or the condition under study may develop. The Investigator must report any significant new findings to the IRB and the IRB will review such findings with regard to potential impact on the subjects' rights and welfare. Since the new knowledge or findings may affect the risks or benefits to subjects or subjects' willingness to continue in the research, the IRB may require, during the ongoing review process that the Investigator contact the currently enrolled subjects to inform them of the new information. The IRB will communicate this to the Investigator. The informed consent should be updated, and the IRB may require that the currently enrolled subjects be re-consented, acknowledging receipt of this new information and for affirming their continued participation. The subject or the subject's legally acceptable representative should be informed in a timely manner if new information becomes available that may be relevant to the subject's willingness to continue participation in the trial. The communication of this information should be documented.

Regulations & Guidance: OHRP Guidance on Written IRB Procedures and 45CFR 46.108(a)(3) and (4); OHRP Guidance on Continuing Review; FDA Information Sheets: Continuing Review after Study Approval

3.8.8 Advertisements

The IRB must approve any and all recruitment materials and/or advertisements prior to posting and/or distribution for studies that are conducted under the purview of the Institutional IRB. The IRB will review:

- The information contained in the advertisement.
- The mode of its communication, including internet-based recruitment.
- The final copy of printed advertisements, prior to posting; and
- The final audio/video taped advertisements.

The IRB reviews the material to assure the material is accurate, and not coercive or unduly optimistic, creating undue influence on the subject to participate which includes, but is not limited to:

- Does not make claims, either explicitly or implicitly, about the drug, biologic, or device under investigation that are inconsistent with FDA labeling.
- Does NOT state or imply a certainty of favorable outcome or other benefits beyond what is outlined in the consent document and the protocol.
- Does NOT promise “free treatment,” when the intent is only to say subjects will not be charged for taking part in the research.
- Does NOT include exculpatory language.
- Does NOT emphasize the payment or the amount to be paid, by such means as larger or bold type.

The advertisement is limited to the information prospective subjects need to determine their eligibility and interest, such as:

- The name and address of the Investigator or research facility
- The condition under study or the purpose of the research
- In summary form, the criteria that will be used to determine eligibility for the study.
- A brief list of participation benefits, if any
- The time or other commitment required of the subjects.
- The location of the research and the person or office to contact for further information.

For FDA-Regulated research, the advertisement:

- Does NOT make claims, either explicitly or implicitly, that the drug, biologic or device is safe or effective for the purposes under investigation.
- Does NOT make claims, either explicitly or implicitly, that the test article is known to be equivalent or superior to any other drug, biologic or device.
- Does NOT use terms, such as “new treatment,” “new medication” or “new drug” without explaining that the test article is investigational.

- Does NOT include a coupon good for a discount on the purchase price of the product once it has been approved for marketing.

Once approved by the IRB, an advertisement cannot be altered or manipulated in any way without prior IRB approval.

Regulations & Guidance: DHHS 45 CFR 46.111(a) (3); 45 CFR 46.116; FDA 21 CFR 50.20; 21 CFR 56.111(a) (3)

3.8.9 Payment to Research Subjects

Payment to research subjects may be an incentive for participation or a way to reimburse a subject for time, travel, parking, and other expenses incurred due to participation. However, payment for participation is not considered a research benefit. Regardless of the form of remuneration, Investigators must take care to avoid coercion of subjects. Subjects are not paid to assume risk but can be compensated for time and effort.

The following regarding payments are described in the protocol and/or initial application:

- Amount
- Method
- Timing of disbursement
- Schedule of all payments
- Credit for payment accrues as the study progresses.

The following must be addressed in the consent or protocol:

- The consent and/or protocol cannot have a statement stating payment is contingent upon completing the entire study.
- The amount of payment and the proposed method and timing of disbursement is neither coercive nor presents undue influence.
- Any amount paid as a bonus for completion is reasonable and not so large as to unduly induce subjects to stay in the study when they would otherwise have withdrawn.
- All information concerning payment, including the amount and schedule of payments, is in the informed consent document.
- Compensation does not include a coupon good for a discount on the purchase price of the product once it has been approved.
- The subject will be informed through the consent process that all payments will come from the LSU payroll department. Subjects may be paid with clin cards

or checks as long as the value of the clin card or check is not coercive. Gift cards and coupons are not acceptable forms of payment.

Pennington Biomedical Research Center has a standard payment schedule for compensation to subjects based on number of visits, type of procedure and time to complete visit procedures. Most studies consider this uniform compensation schedule when assigning a compensation amount for subjects. While the IRB does not approve the Pennington Biomedical compensation schedules; the IRB has the final authority to determine whether compensation is considered coercive. The IRB will review payments to determine that credit for payment accrues as the study progresses.

3.8.10 Recruitment Incentives

Payment arrangements among sponsors, Institutions, Investigators, and those referring research subjects may place subjects at risk of coercion or undue influence or cause inequitable selection. Payment in exchange for referrals of prospective subjects from researchers (physicians) (finder's fees) is not permitted and may be considered illegal under federal or state law. Similarly, payments designed to accelerate recruitment that is tied to the rate or timing of enrollment (bonus payments) also is not permitted. Investigators are strongly encouraged to consult with the IRB office if they have any questions or concerns about recruitment incentives.

3.8.11 Multi-Site Trials Where the Researcher is the Lead Researcher

When the Researcher is the lead Researcher of a multi-site study, the protocol must:

1. Include a plan for how information relevant to the protection of participants will be managed across sites, such as:
    - Unanticipated problems involving risks to participants or others.
    - Interim results
    - Protocol modifications
2. Describe the data and safety monitoring plan that will oversee conduct of the study at all sites. For example,
    a. The frequency of site monitoring visits, who will conduct them and what will occur at each visit.
    b. Schedule of required telephone contacts/conference calls with collaborating site investigators, if applicable. Where and how the data will be stored and for how long. Indicate how the subjects' confidentiality is protected during the transmission of data to other sites.
    c. If records or files are to be transmitted via the internet or shipped to another site, describe how the subjects' confidentiality will be protected.

3.8.12 Transnational Research

Research conducted outside the United States or its territories will generally be subject to approval of a local IRB or Ethics Committee (EC) and/or governmental officials, such as the Ministry of Health. When the research is federally funded, IRB/EC approval must be obtained from an institution/entity in that country that has a current approved FWA and a registered IRB/EC. The IRB will require documentation of the site's IRB approval and FWA/IRB registration status. A database of registered international IRBs searchable by country can be found on the OHRP website at http://ohrp.cit.nih.gov/search/. In addition, OHRP has compiled a listing of the laws, regulations and guidelines that govern human subjects research in many countries around the world (see The International Compilation of Human Subject Research Protections).

3.8.13 Good Clinical Practices

The institution will comply with ICH GCP guidance (E6) only to the extent that it is compatible with NIH, FDA and DHHS regulations in respects to clinical research.

In addition to the requirements outlined in section 3.7.1.1, the IRB considers the following during the initial protocol review:

- Description of the population to be studied.
- References to literature and data that are relevant to the trial, and that provide background for the trial.
- A specific statement of the primary endpoints and the secondary endpoints, if any, to be measured during the trial.
- A detailed description of the objectives and the purpose of the trial.
- A description of the type/design of trial to be conducted (e.g., double-blind, placebo-controlled, parallel design) and a schematic diagram of trial design, procedures and stages.
- A description of the measures taken to minimize/avoid bias, including randomization and blinding.
- A description of the trial treatment(s) and the dosage and dosage regimen of the investigational product(s). Also include a description of the dosage form, packaging, and labelling of the investigational product(s)
- The expected duration of subject participation, and a description of the sequence and duration of all trial periods, including follow-up, if any.
- A description of the "stopping rules" or "discontinuation criteria" for individual subjects, parts of trial and entire trial.

- Accountability procedures for the investigational product(s), including the placebo(s) and comparator(s), if any.
- Maintenance of trial treatment randomization codes and procedures for breaking codes.
- The identification of any data to be recorded directly on the CRFs (i.e., no prior written or electronic record of data), and to be considered to be source data.
- Subject inclusion criteria.
- Subject exclusion criteria.
- Subject withdrawal criteria (i.e., terminating investigational product treatment/trial treatment) and procedures specifying:
    - When and how to withdraw subjects from the trial/investigational product treatment.
    - The type and timing of the data to be collected for withdrawn subjects.
    - Whether and how subjects are to be replaced.
    - The follow-up for subjects withdrawn from investigational product treatment/trial treatment.
- The treatment(s) to be administered, including the name(s) of all the products(s), the dose(s), the dosing schedule(s), the route/mode(s) of administration, and the treatment period(s), including the follow-up period(s) for subjects for each investigational product treatment/trial treatment group/arm of the trial.
- Medication(s)/treatment(s) permitted (including rescue medication) and not permitted before and/or during the trial.
- Procedures for monitoring subject compliance.
- Specification of safety parameters.
- The methods and timing for assessing, recording, and analyzing safety parameters.
- Procedures for eliciting reports of and for recording and reporting adverse event and intercurrent illnesses.
- A description of the statistical methods to be employed, including timing of any planned interim analysis (ses).
- The number of subjects planned to be enrolled. In multicenter trials, the numbers of enrolled subjects projected for each trial site should be specified. Reason for choice of sample size, including reflections on (or calculation of) the power of the trial and clinical justification.
- The level of significance to be used.
- Criteria for the termination of the trial.
- Procedure for accounting for missing, unused, and spurious data.

- Procedures for reporting any deviation(s) from the original statistical plan (any deviation(s) from the original statistical plan should be described and justified in protocol and/or in the final report, as appropriate).
- The selection of subjects to be included in the analyses (e.g., all randomized subjects, all dosed subjects, all eligible subjects, evaluable subjects).
- Specification of the efficacy parameters.
- Methods and timing for assessing, recording, and analyzing of efficacy parameters.

Regulations & Guidance: ICH GCP guidance E6

3.9 Compliance with all Applicable Laws and Regulations

The IRB follows and adheres to all applicable federal, state, and local laws in the jurisdictions where the research is being carried out. The IRB relies on the Pennington Biomedical Research Center Director of Regulatory and Compliance for interpretation and application of federal and state law and the laws of any other jurisdiction where research is conducted as they apply to human subject research.

3.10 Possible IRB Actions

The IRB or reviewer(s) may arrive at the following decisions:

- Approval - see Section 3.10.1.
- Conditional Approval (requiring minor modifications) - see Section 3.10.2.
- Withheld (the IRB has requested major modifications to secure approval) - see Section 3.10.3.
- Disapprove - see Section 3.10.4.
- Suspension or Termination - see Section 3.11.

The following sections provide clarification with respect to each of these decision options.

3.10.1 Approval

Approved: means the determination by the IRB that the investigation and protocol, as submitted, has been reviewed and may be conducted at an institution within the constraints set forth by the IRB and other Institutional and federal regulations. The approval period begins as of the IRB approval date.

Research that has been reviewed and approved by the IRB may be subject to further review depending upon the scope of the research, For example, the Institutional

Biosafety Committee and Institutional Radiation Safety Committee review projects for compliance with biosafety and radiation safety guidelines. The research may be subject to additional institutional requirements before the study can commence.

[DHHS 45 CFR 46.102(h); FDA 21 CFR 56.103(m)].

3.10.2 Conditional Approval

3.10.2.1 Definitions

Conditional Approval: is a situation where the IRB cannot approve the research as submitted or the protocol and/or informed consent document require minor revisions (e.g., wording changes, with replacement language provided). For proposals submitted for convened IRB review, the needed revisions are agreed upon at the IRB meeting. For proposals submitted expedited review, the needed revisions are designated by the IRB Chair (or designee). None of the required modifications can be related to the regulatory criteria for approval. These revisions are presented to the Investigator for incorporation by simple concurrence. Revisions must be made exactly as designated by the IRB or IRB reviewer(s).

3.10.2.2 Policy

To receive an approval following a conditional approval determination the Investigator's response, the revised document(s) (i.e., protocol, informed consent document, etc.) and the tracked document(s) is given to the IRB Chair, and/or a designee of the IRB for review. The reviewer(s) may approve the study upon receipt and approval of the revisions without further action by the IRB. For protocols initially submitted for expedited review, the Investigator's response, the revised document(s) and the tracked document(s) is given to the same reviewer(s) for re-review. The date of the final approval of the submission is the date the conditions were determined to be met.

Approval of the research will not be granted, and certification will not be issued until all deficiencies, if any, are corrected to the satisfaction of the IRB or the reviewer(s).

The outcome of the IRB's deliberations or reviewer(s) findings is communicated to the Investigator in writing. The Investigator may not proceed with the research until receipt of notice of IRB approval of the research.

The IRB's determination concerning the revision will be documented in the minutes of the next regularly scheduled IRB meeting.

An Investigator asking the IRB for review of a “Just-In-Time” grant for funding purposes, should submit an initial application with a protocol and informed consent document. The Investigator is required to prospectively submit the developed study for IRB review and approval prior to identifying, recruiting, or enrolling any subjects in accordance with Department of Health and Human Services (DHHS) 45 CFR 46 (Common Rule), DHHS Standards for Privacy of Individually Identifiable Health Information 45 CFR 160 and 164 (Privacy Rule), and the U.S. Food and Drug Administration (FDA) 21 CFR, parts 50, 56, and 312.

If the IRB approves research with conditions and the research expires before the conditions are reviewed and approved, all research activities must stop until approval is obtained.

3.10.3 Withheld Approval

3.10.3.1 Definitions

Withheld Approval: Made when the research does not meet the IRB criteria for approval. When making this motion, the assigned primary reviewer describes the IRB members’ reasons for the decision and describes recommendations to make the research approvable.

3.10.3.2 Policy

This IRB action is taken if major modification or clarification is required, or insufficient information is provided to adequately judge the protocol application (e.g., the risks and benefits cannot be assessed with the information provided). IRB approval of the proposed research must not occur until subsequent review of the material the Investigator submitted by the convened IRB or the expedited reviewer(s).

For protocols initially submitted for convened IRB review, to receive approval for a Withheld Approval (Major Modifications), the Investigator’s response must be submitted for review at a subsequent, convened meeting of the IRB. The IRB staff provides the IRB with the Investigator’s response, the revised protocol and the previously submitted protocol. The item is placed on the agenda for re-review at the next meeting.

IRB approval of the protocol will not be granted, and an approval letter will not be issued until all deficiencies, if any, are corrected to the satisfaction of the IRB.

The IRB's determination concerning the subsequent amended protocol will be documented in the minutes of the IRB meeting. The outcome of the IRB action is communicated to the Investigator in writing.

3.10.4 Disapproved

The IRB action of Disapproved means that it cannot approve the protocol as written. The IRB has determined that the research cannot:

1. be conducted on Institutional or Pennington Biomedical Research Center premises, or other facilities.
2. cannot involve Pennington employees.
3. be conducted on or by Pennington Biomedical employees.

Notice of the Disapproval will be issued by the IRB in writing.

3.10.4.1 Policy

The IRB will not review research given a Disapproval determination more than twice in a calendar year.

3.10.5 Submitting Requested Changes for New Research Protocol Application with Conditional Approval or a Withheld Determination

If the investigator fails to submit a response to IRB stipulated changes or inquiries related to new research protocols with a conditional approval or withheld approval, the study will remain inactive. The project cannot commence without IRB approval.

3.10.6 Time Limit for Submitting Requested Changes for Continuing Review or Modifications with Conditional Approval or a Withheld Determination

If the IRB approves research with conditions and the research expires before the conditions are reviewed and approved, all research activities must stop until approval is obtained.

3.11 Study Suspension, Termination and Investigator Hold

3.11.1 Suspension or Termination

IRB approval may be suspended or terminated if research is not being conducted in accordance with IRB or regulatory requirements or has been associated with

unexpected problems or serious harm to subjects. (See Policy 8 for a discussion of unanticipated problems and Policy 10 for a discussion of non-compliance)

Suspension of IRB approval is a directive of a convened IRB or the IRB Chair to temporarily stop either some or all previously approved research activities to ensure protection of the rights and welfare of study subjects or for non-compliance. Suspension directives made on an urgent basis by the IRB Chair must be reported to a meeting of the convened IRB. Suspended protocols remain open and require continuing review.

Termination of IRB approval is a directive of the convened IRB to permanently stop some or all activities in a previously approved research protocol. If all research activities are terminated, the research no longer requires continuing review.

The IRB shall notify the Investigator in writing of such suspensions or terminations and shall include an explanation of the reasons for the decision. The Investigator shall be provided with an opportunity to respond in person or in writing.

When a study is suspended or terminated, the convened IRB or authorized individual will:

- Consider actions to protect the rights and welfare of subjects.
- Consider whether procedures for withdrawal of enrolled subjects consider their rights and welfare; and
- Consider informing current subjects of the suspension or termination.
- Have the Investigator report any adverse events or outcomes to the IRB.

Investigators must report to the IRB when a study is suspended or terminated:

- New information that might adversely affect the safety of the participants or the conduct of the clinical trial.
- Any changes significantly affecting the conduct of the clinical trial or increasing the risk to participants.

All suspensions or terminations must be reported to the Institutional Official and reporting agency (if applicable).

Suspension or termination of research that involves an IRB approved protocol also can be issued by Institutional Officials on matters unrelated to the IRB (i.e., not necessarily related to protecting the rights and welfare of study subjects). Such actions can be made by the Executive Director and will be reported to the IRB.

The corrective action(s) and stipulations necessary for the IRB to consider reinstatement of the research must be decided by the convened IRB. The approval will be described in written correspondence to the Principal Investigator.

Regulations & Guidance: DHHS 45 CFR 46.113; FDA 21 CFR 56.113; ICH-GCP (E6)

3.11.2 Investigator Hold

An Investigator or sponsor may request an Investigator hold on a protocol when the Investigator/sponsor wishes to temporarily or permanently stop some or all approved research activities. Investigator holds are not suspensions or terminations.

An administrative hold is a voluntary interruption of research enrollments and ongoing research activities by the researcher.

Suspension of research is defined as a temporary or permanent halt to some or all research procedures until the IRB determines whether the research may recommence (with or without modifications to the research) or whether the research must be terminated. Termination of research means a permanent stop to the research and all research-related activities.

An administrative hold does not apply to interruptions of research related to concerns regarding the safety, rights, or welfare of human research participants, researchers, research staff, or others. If there is an unanticipated problem involving risks to participants or others, the study is not eligible for an administrative hold.

An administrative hold must not be used to avoid reporting deficiencies or circumstances that otherwise require reporting by regulatory agencies.

Activities placed under administrative hold remain subject to continuing review and all organizational policies, such as policies on reporting problems.

An administrative hold cannot be used to extend IRB approval beyond the expiration date of a protocol without IRB approval of continuing review.

An administrative hold may be granted, such as when a researcher goes on extended vacation or takes a leave of absence.

If unavailable to conduct or direct this research personally, as when on leave or vacation, to: (1) arrange for a co-investigator to assume research related responsibilities in the researcher’s absence, and (2) to notify the IRB in writing of this change prior to the absence. If employment with the university is discontinued, to do one of the following with each approved/active study prior to leaving the university: (1)

transfer the study to a new principal investigator or (2) close the project. These changes must be sent in writing to the IRB by submitting either a formal revision or a Continuing Review/Study closure report. This notification must be submitted in advance (prior to the termination of employment).

3.11.2.1 Procedures

Investigators must notify the IRB in writing: providing a description of the research activities that will be stopped; describing proposed actions to be taken to protect current subjects; and describing actions that will be taken prior to IRB approval of proposed changes to eliminate apparent immediate harm.

Upon receipt of written notification from the Investigator, the IRB staff places the research study on the agenda for review. The IRB Chair, in consultation with the Investigator, determines whether any additional procedures need to be followed to protect the rights and welfare of current subjects as described in Protection of Currently Enrolled Subjects below in section 3.11.2.2.

The IRB Chair, in consultation with the Investigator, determines how and when currently enrolled subjects will be notified of the administrative hold.

Investigators may request a modification of the administrative hold by submitting a request for a modification to previously approved research.

3.11.2.2 Protection of Currently Enrolled Subjects

Before an Investigator hold, termination or suspension is put into effect, the convened IRB, IRB Chair (or designee) considers whether any additional procedures need to be followed to protect the rights and welfare of current subjects. Such procedures might include:

- Transferring subjects to another Investigator.
- Making arrangements for clinical care outside the research.
- Allowing continuation of some research activities under the supervision of an independent monitor.
- Requiring or permitting follow-up of subjects for safety reasons.
- Requiring adverse events or outcomes to be reported to the IRB and the sponsor.
- Notification of current subjects; and/or
- Notification of former subjects.

3.12 Continuing Review

The IRB will conduct a continuing review of ongoing research at intervals that are appropriate to the level of risk for each research protocol, but not less than once per year. Continuing review must occur as long as the research remains active for long-term follow-up of subjects, even when the research is permanently closed to the enrollment of new subjects and all subjects have completed all research-related interventions. Continuing review of research must occur even when the remaining research activities are limited to the analysis of private identifiable information.

Regulations & Guidance: DHHS 45 CFR 46.109(e); FDA 21 CFR 56.109(f).

3.12.1 Approval Period

Determination of the approval period and the need for additional supervision and/or participation is made by the IRB on a protocol-by-protocol basis.

For each initial or continuing approval, the IRB will indicate an approval period with an approval expiration date specified. IRB approval is considered to have lapsed at close of business on the expiration date of the approval. For a study approved by the convened IRB, the approval period starts on the date that the IRB conducts its final review of the study; that is, the date that the convened IRB approved the research. For a study approved under expedited review, the approval period begins on the date the IRB Chair (or designee) gives final approval to the protocol.

The approval date and approval expiration date are noted on initial approvals and subsequent continuing review approvals sent to the Investigator and must be strictly adhered to. Investigators should allow sufficient time for development and review of renewal submissions.

Review of a change in research ordinarily does not alter the date by which continuing review must occur. This is because continuing review is review of the full protocol, not simply a change to it.

The regulations make no provision for any grace period extending the conduct of research beyond the expiration date of IRB approval. Therefore, continuing review and re-approval of research must occur by close of business of the date when IRB approval expires.

3.12.2 Continuing Review Process

To assist Investigators, the IRB staff generates courtesy reminders to Investigators approximately 60 days in advance of the study expiration date so that they timely submit continuing reviews. It is the Investigator’s responsibility to ensure that the

continuing review of ongoing research is approved prior to the expiration date. By federal regulation, no extension to that date can be granted.

Information and documentation to be sent to the IRB office by Investigators includes the following:

- Continuing review submission form which includes:
    - A summary since the last IRB review of:
        - Number of Participants accrued.
        - Unanticipated Problems Involving risks to subjects or others.
        - Adverse Events, untoward events, and adverse outcomes experienced by subjects.
        - Subject withdrawals.
        - The reason for withdrawals.
        - Complaints about the research.
        - Amendments or modifications.
        - Any relevant recent literature.
        - Any interim findings.
        - Any relevant multi-center trial reports; and
        - The Investigator's current risk-potential benefit assessment based on study results.
- An assurance that all serious and unexpected adverse events had been reported as required. The current IRB-approved informed consent document.
- Newly proposed consent with redline edits (i.e., additions are to be underlined, deletions are to be lined through) to reflect any changes from the prior submission.
- The current IRB-approved protocol.

In conducting continuing review of research not eligible for expedited review, all IRB members will have the last approved consent and the continuing review report. The primary reviewer receives all the previous listed materials (see section 3.5.4). At the meeting, the primary reviewer leads the IRB through the completion of the regulatory criteria for approval. (See section 3.5.3)

The IRB staff attends the convened meetings and ensures that the proposed study documents (consent, protocol, IB, application, supporting documents) for each protocol on the agenda have been distributed to the IRB members appropriately. The IRB staff will retrieve any additional materials should the IRB members or reviewer(s) request.

Review of currently approved or newly proposed consent documents must occur during the scheduled continuing review of research by the IRB. However, informed

consent documents should be reviewed whenever new information becomes available that would require modification of information in the IRB approved informed consent document. Changes to consent documents are modifications and will be reviewed according to the procedures in section 3.13 – Modification of an Approved Protocol.

Continuing review of a study must continue until:

- The research is permanently closed to the enrollment of new subjects.
- All subjects have completed all research related interventions.
- Collection and analysis or private identifiable information has completed.

3.12.3 Expedited Review of Continuing Review

In conducting continuing review under expedited review, at least one qualified IRB member is provided and reviews the Continuing Review submission form and complete protocol. At least one reviewer receives and reviews the same materials that the IRB receives for protocols reviewed by the convened IRB:

- Current consent document, if applicable.
- A status report on the progress of the research (broader than modifications and adverse events).

The status report on the progress of the research must include:

- Number of participants accrued.
- A summary since the last IRB review of:
    - Unanticipated problems involving risks to participants or others.
    - Participant withdrawals.
    - The reasons for withdrawals.
    - Complaints about the research.
    - Any relevant recent literature.
    - Any interim findings.
    - Any relevant multi-center trial reports.
    - The researcher's current risk-potential benefit assessment based on study results.
    - A summary of modifications previously approved, if applicable.
    - Deviation log, if applicable.

Generally, if research did not qualify for expedited review at the time of initial review, it does not qualify for expedited review at the time of continuing review, except in limited circumstances described by expedited review paragraphs (8) and (9) found in section 3.4.2 -Expedited Review Categories. It is also possible that research activities that

previously qualified for expedited review in accordance with 45 CFR 46.110, have changed or will change, such that expedited review would no longer be permitted for continuing review.

Additionally, continuing review of research previously approved by the convened IRB may be conducted using the expedited review procedure where the research is not conducted under an investigational new drug application (IND) or investigational device exemption (IDE) where categories two (2) through eight (8) do not apply but the IRB determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified since the last review.

3.12.4 Lapse in Continuing Review Approval

The regulations permit no grace period or approval extension after approval expiration. Research that continues after the approval period has expired is considered to be research conducted without IRB approval. If the continuing review approval does not occur within the timeframe set by the IRB, this is a lapse in continued review approval. All research activities must stop. This includes cessation of subject recruitment (e.g., media advertisements must be pulled), enrollment, consent, interventions, interactions, and data collection, unless the IRB finds that it is in the best interests of individual subjects to continue participating in the research interventions or interactions. This will occur even if the Investigator has provided the required information for continued review before the expiration date. Therefore, Investigators must allow sufficient time for IRB review and approval.

It is the responsibility of the Investigator to ensure that a lapse in approval does not occur. The IRB staff will notify the Investigator of the expiration of approval and that all research activities must cease unless the IRB determines that stopping the intervention would cause immediate harm subjects.

If research subjects are currently enrolled in the research project and their participation is ongoing, once notified of the expiration of approval, the Investigator must immediately submit to the IRB Chair a list of research subjects for whom suspension of the research would cause harm. Enrollment of new subjects cannot occur and continuation of research interventions or interactions for already enrolled subjects will only continue when either the IRB or IRB Chair finds that it is in the best interest of the individual subjects to do so.

Failure to timely submit continuing review information is considered non-compliance by the Investigator and will be handled according to the non-compliance policy (see Policy 10 - Non-Compliance).

Once approval has expired (i.e., lapse in continuing review approval), IRB review and re-approval must occur prior to re-initiation of the research.

3.13 Modification of an Approved Protocol

Investigators who wish to modify or amend their approved research must seek IRB approval before making any changes in approved research. This requirement exists even though the changes are planned for the period for which IRB approval has already been given. One noteworthy exception is for changes necessary to eliminate an immediate hazard to the subject, in which case the IRB must then be notified at once.

Modifications may be approved if they are within the scope of what the IRB originally authorized. For example, if a researcher wishes to add a population to an existing study, but not alter the study procedures or purpose, a modification request is appropriate. Likewise, modifying a procedure without changing the study's purpose or study population may also be appropriate.

Investigators must submit documentation to inform the IRB about the changes in the status of the study. To this end, Investigators are required to submit the changes to the IRB office. The following completed forms must be turned in:

- Application for a modification; revised sponsor’s protocol (if applicable)
- Revised approved consent /assent documents (if applicable) or other documentation that would be provided to subjects when such information might relate to their willingness to continue to participate in the study.
- Revised or additional recruitment materials; or any other relevant documents provided by the Investigator.

The reviewer(s) using the expedited procedure has the ultimate responsibility to determine that the proposed changes may be approved through the expedited review procedure and, if not, must refer the protocol for convened IRB review. (See 3.13.1 Expedited Review of Protocol Amendments/Modifications)

Regulations & Guidance: OHRP Guidance on Written IRB Procedures and 45CFR 46.108(a)(3) and (4).

3.13.1 Expedited Review of Protocol Amendments/Modifications

An IRB may use expedited review procedures to review minor changes in ongoing previously approved research during the period for which approval is authorized. An

expedited review may be carried out by the IRB Chair and/or designee(s) among the IRB members.

The reviewer(s) determine whether the modifications meet the criteria allowing review using the expedited procedure, and if so, whether the research with the proposed modifications continues to meet the regulatory criteria for approval.

The reviewer will also consider whether information about those modifications might relate to subjects' willingness to continue to take part in the research and if so, whether to provide that information to subjects.

One tracked copy or a summary should show all changes from the previous version (i.e., underlining all additions and striking through all deletions). The protocol must include the title and version date.

3.13.2 Convened IRB Review of Protocol Modifications

When a proposed change in a research study is not minor (e.g., procedures involving increased risk or discomfort are to be added), then the IRB must review and approve the proposed change at a convened meeting before the change can be implemented. The only exception is a change necessary to eliminate apparent immediate hazards to the research subjects. In such a case, the IRB should be promptly (no longer than within 30 days) informed of the change following its implementation and should review the change to determine that it is consistent with ensuring the subjects' continued welfare.

All documents provided by the Investigator are given to the primary reviewer (see section 3.5.3 - Primary Reviewers)

At the meeting, the primary reviewer presents an overview of the modification(s) and leads the IRB through the completion of the regulatory criteria required for approval. The IRB will determine whether the research with the proposed modifications continues to meet the regulatory criteria for approval.

When the IRB reviews modifications to previously approved research, the IRB considers whether information about those modifications might relate to subjects' willingness to continue to take part in the research and if so, whether to provide that information to subjects.

One tracked copy or a summary should show all changes from the previous version (i.e., underlining all additions and striking through all deletions). The protocol must include the title and version date.

3.13.3 Changes in the Informed Consent Document

When a modification makes it necessary to change the informed consent document, regardless of whether any subjects are enrolled, two copies of the revised consent document are to be submitted to the IRB. One tracked copy should show all changes from the previous version (i.e., underlining all additions and striking through all deletions). The one clean copy will contain the IRB approval stamp without any outdated text.

3.14 Closure of Protocols

The completion or termination of a study is a change in activity that must be reported by the Investigator to the IRB on the closure report. Although subjects will no longer be at risk under the study, a final report to the IRB allows it to close the study files as well as provide information that may be used by the IRB in the evaluation and approval of related studies involving the Investigator.

The Investigator should submit the closure report to the IRB office. IRB staff will review the closure application for completeness and will notify the IRB. Closure applications in which the protocol will expire prior to the next scheduled IRB meeting will be closed and the final report will be included on the next agenda as a closure item. If the study is closed prematurely, it must be reported to the IRB.

3.15 Notice to Investigators of IRB Actions

Barring extraordinary circumstances, all IRB action letters are generated through IRBManager and sent to the Investigator and research team within ten (10) working days. For an approval, along with written notification of approval, a copy of the approved consent document(s) containing the stamped approval with the dates of the approval and expiration on each sheet will be attached. For conditional approval requiring modifications, the notification will include the information that must be modified. For a disapproval, termination or suspension, the notification will include the basis for making that decision.

Before initiating a trial, the investigator should have written and dated approval from the IRB for the protocol, written informed consent form, consent form updates, subject recruitment procedures (e.g., advertisements), and any other written information to be provided to subjects.

All correspondence between IRB and Investigators are retained in the study file.

When the IRB requires modifications to research, investigators' responses will be reviewed to verify that the conditions for approval have been satisfied. Depending on the nature of the modifications, this subsequent review/verification may be performed by the IRB Chair and/or designee or a consultant with specific expertise. Questions about whether the conditions for approval have been satisfied will be forwarded to the IRB Chair. When the conditions for approval are not met the submission will be reviewed again by the same method as the original review (i.e., convened, or expedited review).

The IRB reports its findings and actions to the Institution in the form of IRB minutes, a copy of which is distributed by IRB staff to Institutional Officials with a copy stored in the IRB files.

3.16 Appeal of IRB Decisions

When an IRB protocol presented at a convened meeting is disapproved or given a Withheld Approval, the IRB will notify the Investigator in writing about the specific deficiencies and/or the modifications that are necessary for appropriate IRB approval. The IRB shall include in its written notification a statement of the reasons for its decision and give the Investigator an opportunity to respond in writing. The Investigator also is given the opportunity to schedule a meeting with the IRB to discuss this matter. If the matter will be presented to the convened board, the IRB staff will notify the researcher of the convened board meeting date.

In cases where there is disagreement between the IRB and the Investigator regarding the nature and extent of the requested changes and these disagreements cannot be resolved amicably in an informal manner, the Investigator and/or the IRB may make an appeal to the Institutional Official for a resolution of the matter. The Institutional Official may organize a meeting to help facilitate discussion between the IRB and the Investigator. While the Institutional Official may provide input and make recommendations to the IRB for expeditious resolution of the matter, final recommendations for approval remain under the purview of the IRB.

Specific questions regarding the IRB policies and procedures can be submitted by email, writing and/or via the telephone to the IRB office for further information and/or clarification.

Regulations & Guidance: DHHS 45 CFR 46.109(d); FDA 21 CFR 56.109(e)

4.0 Documentation and Records

4.1 Policy

Pennington Biomedical Research Center shall prepare and maintain adequate documentation of IRB activities. All records must be accessible for inspection and copying by authorized representatives of the FDA, OHRP, sponsors, and other authorized entities at reasonable times and in a reasonable manner.

4.2 Definitions

Research records: consists of records prepared, created, gathered, or maintained by an investigator or research staff for research at the institution.

4.3 IRB Records

IRB records include, but are not limited to:

- Written operating procedures
- IRB membership rosters (See Section 4.5).
- IRB member training records. The IRB maintains accurate records listing IRB members and IRB staff that have fulfilled the institution's human subject training requirements. All Pennington Biomedical employees' (investigators, administration, and support staff) human research protections training are coordinated by the Director of Legal and Regulatory Compliance. Outside investigators involved in research are required to show proof of human subjects training to the IRB before study approval
- IRB member occupations/affiliations
- IRB correspondence (other than protocol related)
- IRB study files (See Section 4.4 for information included in study files)
- Documentation of exemptions (See Section 4.7)
- Documentation of convened IRB meetings minutes (see Section 4.6 for information included in the minutes)
- Documentation of review by another institution's IRB when appropriate
- Documentation of cooperative review agreements
- Federal wide assurances
- Quality assurance reviews
- Workflow/SOPs
- Applicable GCP regulatory requirement(s)

Regulations & Guidance: DHHS 45 CFR 46.115(a)-(b); FDA 21 CFR 56.115(a)-(b), ICH-GCP (E6)

4.4 IRB Study Files

The IRB office will maintain a study file for each IRB study submission that is submitted for review. Once a study submission is confirmed to include appropriate submission materials and signature of investigator(s), it is assigned a unique IRB number by the IRB staff.

All communications to and from the IRB are maintained. Depending on the type of communication, maintenance may be via paper or electronically. IRB study files include, but are not limited to:

1. Protocol and all other documents submitted as part of an initial IRB application
2. Protocol and all other documents submitted as part of a request for continuing review/closure report. This also includes progress reports, statements of significant new findings provided to subjects, reports of injuries to patients
3. Documents submitted and reviewed after the study has been approved, including reports of modifications to research and unanticipated problem reports
4. Copy of the IRB-approved consents/assents
5. Sponsor-approved sample consent form document and protocol, when they exist
6. IRB member reviewer forms
7. Documentation of type of IRB review
8. For expedited review, documentation of any determinations required by the regulations and protocol-specific findings supporting those determinations, including: waiver or alteration of the consent process, research involving pregnant women, neonates, and research involving children
9. Documentation of all IRB review actions
10. Notification of suspension of research, if applicable
11. Correspondence pertaining to appeals/grievances, if applicable
12. Copies of approval letters and forms that describe what investigators must have before beginning the study
13. IRB correspondence to and from investigators
14. All other IRB correspondence related to the research
15. Reports of unanticipated problems
16. Documentation of audits, investigations, reports of external site visits
17. Scientific evaluations
18. DHHS-approved sample consent document and protocol, when they exist
19. Protocol Deviations/Violations/Exceptions
20. Documentation of non-compliance

21. Investigator Brochure, if any
22. Recruitment materials
23. Data and safety monitoring reports, if any
24. Records may be maintained in printed form or electronically 45 CFR 46 115(b)
25. For Studies approved after January 21, 2019 which do not require continuing review, a status report is required. 45 CFR 46.115(a)(3)
26. For an expedited reviewer's determination that research appearing on the expedited review list is more than minimal risk, records must include the rationale, per 45 CFR 46115(a)(8)
27. Records must include documentation specifying the responsibilities that a relying organization and an organization operating an IRB will undertake to ensure compliance with the requirements of the Common Rule. 45 CFR 46 115 (a) (9)
28. Records must include the rationale for conducting continuing review on research that otherwise would not require continuing review.

Regulations & Guidance: FDA 21 CFR 56.115(a), 45CFR46.108(a)(2)

4.5 IRB Membership Roster

A membership list of IRB members must be maintained for each IRB committee. It must identify members sufficiently to describe each member's chief anticipated contributions to IRB deliberations. The list must contain the following information about IRB members:

1. Name
2. Earned degrees
3. Affiliated or non-affiliated status (neither the member nor an immediate family member of the member may be affiliated with the institution)
4. Employment or other relationship between each IRB member and Pennington Biomedical Research Center
5. Status as scientist (physician-scientist, other scientist, non-scientist or social behavioral scientist). For purposes of this roster, IRB members with research experience are designated as scientists. Research experience includes training in research (e.g., doctoral degrees with a research-based thesis) and previous or current conduct of research.
6. Indications of experience, such as board certifications or licenses sufficient to describe each member's principal anticipated contributions to IRB deliberations
7. Representative capacities of each IRB member; which IRB members are knowledgeable about or experienced in working with children, pregnant women, , individuals with impaired decision-making capacity, and other vulnerable populations locally involved in research
8. Role on the IRB (e.g., IRB Chair, etc.)

9. Voting status. Note that all IRB members are, by definition, entitled to vote. Guests and non-voting member's guests do not have a right to vote or be counted toward a quorum
10. Alternate member status, including the IRB member for whom they alternate with

The IRB office must keep the IRB membership list current. IRB records including a curriculum vitae and human subjects' protection training of each IRB member. The IRB staff must promptly report changes in IRB membership to OHRP.

Regulations & Guidance: FDA 21 CFR 56.115(a).

4.6 IRB Minutes

Actions by duly convened IRB proceedings must be reduced to writing and are available for review generally within 3 weeks of the recorded meeting date. Once approved by the IRB at a subsequent IRB meeting, the minutes must not be altered by anyone including a higher institutional authority. It should be noted that errors or corrections to approved IRB minutes, as approved by a majority of the convened IRB, will be included in the next meeting minutes.

A copy of IRB approved minutes for each IRB meeting is distributed to the designated Institutional Official.

Minutes of IRB meetings must contain sufficient detail to show:

1. Names of IRB members present
2. Names of IRB members or IRB alternate members who are participating through videoconference, teleconference or other electronic means, and documentation that those not physically present have received all pertinent material prior to the meeting and were able to actively and equally participate in all discussions
3. Names of absent IRB members
4. Names of alternates attending in lieu of specified (named) absent IRB members. Alternates may substitute for specific absent members only as designated on the official IRB membership roster
5. Names of consultants present, if applicable
6. Name of investigators or research staff present
7. Names of guests present
8. The attendance list shall include those members present at the meeting. The minutes will indicate, by name, those members who enter or leave the meeting. The vote on each action will reflect those members present for the vote on that item;

9. The presence of a quorum initially and throughout the IRB meeting, including the presence of one member whose primary concern is in a non-scientific area;
10. Business items discussed;
11. Continuing education conducted;
12. Actions taken, including separate deliberations, actions, and votes for each protocol undergoing initial review, continuing review, or review of modifications by the convened IRB;
13. Votes on these actions (total number voting; number voting for; number voting against; number abstaining; number of those excused, number of those recused);
14. Basis or justification for all IRB actions and/or decisions including required changes in research or disapproval;
15. Summary of controverted issues and their resolution;
16. Approval period for initial and continuing review protocols, including identification of research that warrants review more often than annually and the basis for that determination;
17. Risk level of initial and continuing review approved protocols;
18. Review of interim reports (e.g. adverse events or safety reports; amendments; report of violations or deviations, etc.);
19. Review of DSMB summaries;
20. Review of DSMB plans;
21. Applications that have met or not met the stipulations;
22. Justification of deletion or modifications of information concerning risks or alternative procedures contained in the DHHS-approved sample consent document;
23. Protocol-specific documentation that the research meets the required criteria [45 CFR 46.116(d)] when approving a consent procedure that does not include or that alters some or all of the required elements of informed consent, or when waiving the requirement to obtain an informed consent;
24. Protocol-specific documentation that the research meets the required criteria [45 CFR 46.117(c)] when the requirements for documentation of consent are waived;
25. When approving research that involves populations covered by subparts B or D of 45 CFR 46, the minutes will document the IRB justifications and findings regarding IRB determinations stated in the Subparts or the IRB agreement with the findings and justifications as presented by the investigator on IRB forms;
26. The rationale for significant risk device/non-significant device determinations;
27. COI determinations;
28. Identification of any research for which there is need for verification from sources other than the investigator that no material changes are made in the research (e.g., cooperative studies, or other collaborative research);

29. Special protections warranted in specific research projects for groups of subjects who are likely to be vulnerable to coercion or undue influence, such as children, pregnant women, , individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, regardless of source of support for the research;
30. A list of research approved since the last meeting utilizing expedited review procedures and the specific citation for the category of expedited review of the individual protocol;
31. Documentation of approval by the IRB Chair (or designee) of research contingent on specific minor conditions in the minutes of the first IRB meeting that takes place after the date of the approval;
32. An indication that, when an IRB member has a COI (see section 2.5 – IRB Member Conflict of Interest) with the research under review, the IRB member was not present during the deliberations or voting on the proposal, and that the quorum was maintained. The name of the IRB member will be captured in the minutes as well as the reason for their departure; and
33. Key information provided by consultants will be documented in the minutes or in a report provided by the consultant.
34. Actions taken by the IRB, include documenting the criteria for approval are met.

IRB minutes are audited every quarter to ensure all items are included.

Regulations & Guidance: 45 CFR 46.116(c)-(d); 45 CFR 46.117(c); 45 CFR 46.204; 45 CFR 46.205; 45 CFR 46.206; 45 CFR 46.207; 45 CFR 46.305; 45 CFR 46.306; 45 CFR46.404; 45 CFR 46.405; 45 CFR 46.406; 45 CFR 46.407; 45 CFR 46.408; 42 USC 498 A(b)(1); 42 USC 498 A(b)(2); 42 USC 498 A(c); FDA 21 CFR 50.51; 21 CFR 50.52; 21 CFR 50.53; 21 CFR 50.54; 21 CFR 50.55; 21 CFR 50.56; 21 CFR 56.109(c); 21 CFR 56.115(a)

4.7 Documentation of Exempt Review Findings

Documentation of exempt review consists of the reviewer's citation of a specific exemption category and written concurrence by the IRB of the activity.

4.8 Documentation of Expedited Reviews

IRB records for initial and continuing review by the expedited procedure must include:

1. The specific permissible category;
2. A description of action taken by the reviewer;
3. The approval period; and

4. Any determinations required by the regulations including protocol-specific findings supporting those determinations.

4.9 Access to IRB Records

The IRB has policies and procedures to protect the confidentiality of research information:

1. All paper IRB records are kept secure in filing cabinets or locked storage rooms. The IRB office is closed and locked when unattended.
2. Access to IRB records, whether paper or electronic, is limited to the IRB Chair, IRB members, IRB staff, authorized institutional officials, and officials of federal and state regulatory agencies (OHRP, FDA). Research investigators are provided reasonable access to files related to their research. Appropriate accreditation bodies are provided access and may recommend additional procedures for maintaining security of IRB records. All other access to IRB records is limited to those who have legitimate need for them, as determined by the institutional official.
3. Records are accessible for inspection and copied by authorized representatives of federal regulatory agencies during regular business hours.
4. Paper records may not be removed from the IRB office; however, the IRB staff will provide copies of records for authorized personnel if requested.
5. All other access to IRB study files, paper or electronic, is prohibited.

4.10 Record Retention

IRB records (as described in Section 4.3) pertaining to research, which is conducted, must be stored securely. Paper records are stored in the IRB office.

IRB records must be retained for at least three (3) years after completion of the research. IRB records not associated with research or for protocols cancelled without subject enrollment will be retained at the facility for at least 3 years after closure of the IRB file.

IRB records retained beyond their retention date will be shredded or otherwise destroyed unless prohibited by institutional policy.

See Section 4.12 for record retention requirements for studies involving investigational drugs and investigational devices.

Regulations & Guidance: DHHS 45 CFR 46.115(b); FDA 21 CFR 56.115(b); 21 CFR 56.312.62(c)

4.11 Investigator Records

Investigators are required to maintain accurate, current and complete records of their human subject research activities. In general, investigators should establish and maintain a file for each study that has been reviewed by the IRB. These files should closely resemble the IRB's file structure on the study.

Within each study, investigators also should maintain a file for each subject who signs a consent document agreeing to participate in the study. These subject-specific files should include the original signed consent document and copies of case report forms, and any other correspondence between the investigator and the subject.

All clinical trial information should be recorded, handled, and stored in a way that allows its accurate reporting, interpretation and verification. This principle applies to all records referenced in this guideline, irrespective of the type of media used.

Research records should be maintained as appropriate to the type of study. For example, when a study is sponsored externally, these records should be kept for at least 3 years after the study has been completed and the sponsor has indicated that the records are no longer required.

4.12 Records for FDA-Regulated Studies

4.12.1 Investigational Drugs

Investigators are expected to maintain accurate, complete and current records with respect to studies involving investigational drugs consistent with FDA requirements found at 21 CFR 312.62(a)(b)(c). This includes the following:

1. Disposition of drug: an investigator is required to maintain adequate records of the disposition of the drug, including dates, quantity, and use by subjects.
2. Case histories: an investigator is required to prepare and maintain adequate and accurate case histories that record all observations and other data pertinent to the investigation on each individual that administered the investigational drug or employed as a control in the investigation. Case histories include the case report forms and supporting data including (e.g., signed and dated consent forms), and medical records (e.g., physician progress notes, the individual's hospital chart(s), and the nurses' notes). The case history for each individual shall document that informed consent was obtained prior to participation in the study.
3. Record retention: an investigator shall retain records involving investigational drugs involved in an FDA-regulated study for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being

investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.

Regulations & Guidance: FDA 21 CFR 312.62.

4.12.2 Investigational Devices

Investigators must maintain accurate, complete and current records involving investigational devices involved in an FDA-regulated study consistent with FDA requirements found at 21 CFR 812.140(a)(d). This includes the following:

1. All correspondence with another investigator, an IRB, the sponsor, a monitor, or FDA, including required reports;
2. Records of receipt, use or disposition of a device that relate to:
    a. The type and quantity of the device, the dates of its receipt, and the batch number or code mark.
    b. The names of all persons who received, used, or disposed of each device.
    c. Why and how many units of the device have been returned to the sponsor, repaired, or otherwise disposed of.
3. Records of each subject's case history and exposure to the device. Case histories include the case report forms and supporting data (e.g., signed and dated consent forms) and medical records (e.g., physician progress notes, copies of individual's hospital chart(s), and the nurses' notes). Such records shall include:
    a. Documents, evidencing informed consent and, for any use of a device by the investigator without informed consent, any written concurrence of a licensed physician and a brief description of the circumstances justifying the failure to obtain informed consent. The case history for each individual shall document that informed consent was obtained prior to participation in the study.
    b. All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.
    c. A record of the exposure of each subject to the investigational device, including, the date and time of each use, and any other therapy.
4. The protocol with documents showing the dates of and reasons for each deviation from the protocol.
5. Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

5.0 Obtaining Informed Consent from Research Subjects

5.1 Policy

No investigator conducting research at Pennington Biomedical Research Center may involve a human subject in research without obtaining the legally effective informed consent of the subject or the subject's legally authorized representative unless a waiver of consent has been approved by the IRB in accordance with section 5.10 of these procedures. Except as provided in section 5.12, informed consent must be documented by the use of a written consent form approved by the IRB (see section 5.7).

The IRB will evaluate both the consent process and the procedures for documenting informed consent to ensure that adequate informed consent is obtained from subjects.

The following procedures describe the requirements for obtaining consent from subjects in research at Pennington Biomedical Research Center.

Regulations & Guidance: DHHS 45 CFR 46.116; FDA 21 CFR 50.20

5.2 Basic Requirements

Informed consent must be obtained by the investigator (or properly trained designee) prior to entering or enrolling a subject into an IRB approved study and/or conducting any study related procedures required by the protocol, unless consent is waived by the IRB.

If someone other than the investigator conducts the interview and obtains consent from the subject, the investigator needs to formally delegate this responsibility, and the person so delegated must have received appropriate training to perform this activity. The person so delegated must be knowledgeable about the research to be conducted and the consenting process, and must be able to answer questions about the study.

These informed consent requirements are not intended to preempt any applicable federal, state or local laws that require additional information to be disclosed for informed consent to be legally effective.

All consents under the purview of Pennington Biomedical Research Center IRB must be on the Pennington Biomedical Research Center consent template format located on the HRPP website. Sample or draft consent documents may be developed by a sponsor or cooperative study group; however, they must be in the Pennington Biomedical Research Center consent template.

Regulations & Guidance: FDA 21 CFR 50.20.

5.3 Securing and Documenting Informed Consent

An investigator (or properly trained designee) is required to obtain legally effective informed consent from a subject or the subject's legally authorized representative. DHHS 45 CFR 46.177; FDA 21 CFR 50.20

When informed consent is required, it must be sought prospectively, and properly documented according to legal and regulatory requirements. DHHS 45 CFR 46.117; FDA 21 CFR 50.20

The requirement to obtain the legally effective informed consent of individuals before involving them in research is one of the central protections provided for by the federal regulations and the IRB Office.

The informed consent process involves three key features:

- Disclosing to the prospective human subject information needed to make an informed decision
- Facilitating the understanding of what has been disclosed
- Promoting the voluntariness of the decision about whether or not to participate in the research.

Informed consent is more than just a signature on a form. It is a process of information exchange to include reading and signing the informed consent document. The informed consent process is the critical communication link between the prospective human subject and an investigator, beginning with the initial approach of an investigator and continuing through the completion of the research study. Investigators must have received the appropriate training and be knowledgeable about the study protocol in order that they may answer questions to help provide understanding to the study subject or potential study subject. The exchange of information between the investigator and study subject can occur via one or more of the following modes of communication, among others; face to face contact, mail; telephone; or fax.

5.4 Informed Consent Process

Informed consent must be obtained under the following circumstances:

- Informed consent may only be obtained from subjects who have the legal and mental capacity to give consent. For subjects without that capacity, consent must be obtained from a legally authorized representative.
- The informed consent process shall be sought under circumstances that provide the subject (or legally authorized representative) with sufficient opportunity to consider

whether or not to participate. The researcher must give either the participant or the representative adequate opportunity to read the consent document before it is signed.

- The informed consent process shall be sought under circumstances that minimize the possibility of coercion or undue influence. Coercion occurs when an overt or implicit threat of harm is intentionally presented by one person to another in order to obtain compliance. Undue influence, by contrast often occurs through an offer of an excessive or inappropriate reward or overture in order to obtain compliance.
- The informed consent information must be presented in language that is understandable to the subject (or legally authorized representative). To the extent possible, the language should be understandable by a person who is educated to 8th grade level and layman's terms shall be used in the description of the research.
- For subjects whose native language is not English, informed consent must be obtained in a language that is understandable to the subject (or legally authorized representative). In accordance with this policy, the IRB requires that informed consent conferences include a qualified translator when the prospective subject does not understand the language of the person who is obtaining consent.
- After the written informed consent form and any other written information to be provided to participants, is read and explained to the participant or the participant's legally authorized representative, and after the participant or the participant's legally authorized representative has orally consented to the participant's participation in the trial and, if capable of doing so, has signed and personally dated the informed consent form, the person administering the consent should sign and personally date the consent form.
- By signing the consent form, the person administering the consent attests that the information in the consent form and any other written information was accurately explained to, and apparently understood by, the participant or the participant's legally authorized representative, and that informed consent was freely given by the participant or the participant's legally authorized representative.
- In accordance with the American Disabilities Act, Pennington Biomedical Research Center will provide any assistance to any subject with a disability. For hearing impaired subjects, Pennington Biomedical will provide hearing impaired equipment or a translator. For subjects with a visual impairment, an impartial witness must be present during the informed consent process if the subject does not have a legally authorized representative.
- For subjects that are illiterate, an impartial witness to the subject will sign as a reader unless the subjects legally authorized representative is present.
- The informed consent process may not include any exculpatory language through which the subject is made to waive, or appear to waive any of the subject's legal rights or through which the Investigator, the Sponsor, the Institution or Pennington

employees or institutional agents are released from liability for negligence, or appear to be so released. DHHS 45 CFR 46.116; FDA 21 CFR 50.20

- The investigator is ultimately responsible for ensuring that each prospective subject is adequately informed about all aspects of the research and understands the information provided. However, the IRB office, the research investigators and the research staff all share in the responsibility of ensuring that the informed consent process is adequate.
- Federal regulations do not specify how far in advance of study entry a subject can provide consent. The amount of time required by a subject to make a decision would presumably depend upon the nature of the study, taking into consideration the degree of risk, potential benefits, alternatives, and desire to consult with family. For the sake of clarification, consents are current for 30 days but it may be prudent to review information contained in the consent document with the research subject prior to initiating any research procedures.
- Neither the investigator, nor the trial staff, should coerce or unduly influence a subject to participate or to continue to participate in a trial.

Regulations & Guidance: DHHS 45 CFR 46.109(b); 45 CFR 46.116, 117; FDA 21 CFR 50.25; 21 CFR 56.109(b); OHRP Guidance on Exculpatory Language in Informed Consents; FDA Information Sheets: A Guide to Informed Consents

5.5 Basic Elements of Informed Consent

To be valid, the consent process must provide the following basic elements of information to potential subjects, which includes:

- A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental and done for research purposes; a description of any reasonably foreseeable risks or discomforts to the subject including privacy risks (legal, employment, etc.).
- A description of any benefits to the subject or to others which may reasonably be expected from the research.
- The alternative procedures or treatment that might be available to the participant, and their important potential benefits and risks.
- A statement describing the extent, if any, to which confidentiality of records identifying the subject must be maintained.
- For research involving more than minimal risk, an explanation as to the availability of medical treatment in the case of research related injury, including who will pay for the treatment and whether other financial compensation is available.

- An explanation of whom to contact on the research team for answers to pertinent questions about the research or to voice concerns or complaints about the research, and whom to contact in the event of a research-related injury to the subject.
- Contact information for the IRB to obtain answers to questions about the research; to voice concerns or complaints about the research; to obtain answers to questions about their rights as a research subject; in the event the research staff could not be reached; and in the event the subject wishes to talk to someone other than the research staff.
- A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

Under the 2018 Final Rule, the basic elements have been expanded in 116(b) to include 3 *new requirements*.

- When appropriate, informed consent must include the following:
    - A statement that biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit (.116(c)(7));
    - A statement about whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions (.116(c)(8));
    - A statement about whether the research project will or might include whole genome sequencing (.116(c)(9)).

***New* Requirements to Informed Consent Process and Document** are meant to facilitate subjects' understanding of the reasons to participate (or not) in the research). It requires that key information essential to decision making receive priority by:

- Being presented first in the consent discussion; and
- Appearing at the beginning of the consent document
- Prospective subject (or LAR) must be provided with the information that a reasonable person would want to have to make an informed decision about whether to participate, and be given an opportunity to discuss that information. (.116(a)(5)(i))
- Informed consent must begin with "a concise and focused presentation of the ***key information*** that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research." (§____.116(a)(5)(i)).

- This statement “must be organized and presented in a way that facilitates comprehension.” (§____.116(a)(5)(i)).

The Key Information Section*:* According to the preamble of the Final Rule, a brief description of five “factors” (elements) at the beginning of an informed consent process (and consent form) would encompass the key information including a concise explanation of the following (HHS 2017, 7149-274):

(1) The fact that consent is being sought for research and that participation is voluntary
(2) The reasonably foreseeable risks or discomforts to the prospective subject
(3) The purposes of the research, expected duration of the prospective subject’s participation, and procedures to be followed in the research
(4) The benefits to the prospective subject or others that may reasonably be expected from the research
(5) Appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the prospective subject.

Electronic consent is allowed if subjects are provided a written copy.

Screening, recruiting, determining eligibility. IRBs do not need to obtain informed consent in instances of obtaining information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects, under certain circumstances. (§ ____.116(g)).

For research involving collection of identifiable private information or identifiable biospecimens. In these instances, subjects should be provided with:

- A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens; and
- The information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent, where applicable; or
- A statement that the subject’s information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies. (§ ____.116(b)(9)).

Regulations & Guidance: DHHS 45 CFR 46.116(a); FDA 21 CFR 50.25(a); OHRP Guidance on Exculpatory Language in Informed Consents; FDA Information Sheets: A Guide to Informed Consents; Consent Template found on the HRPP website

5.6 Additional Elements of Informed Consent to be applied, as appropriate:

Additional situational-specific elements that an informed consent should include are:

- A statement that the particular treatment or procedure may involve risks to the subject, which are currently unforeseeable. (e.g., include when the research involves procedures in which the risks to subjects are not well known).
- A statement that if the subject is or becomes pregnant, the particular treatment or procedure may involve risks to the embryo or fetus, which are currently unforeseeable (e.g., include when the research involves pregnant women or women of childbearing potential and the risk to fetuses of the drugs, devices, or other procedures involved in the research is not well known).
- Anticipated circumstances under which the subject's participation may be terminated by the Investigator without regard to the subject's consent.
- Any additional costs to the subject that may result from participation in the research;
- The consequences of a subject's decision to withdraw from the research (e.g., include when withdrawal from the research is associated with adverse consequences).
- Procedures for orderly termination of participation by the subject.
- A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject (e.g., include when the research is long term and interim information is likely to be developed during the conduct of the research).
- The approximate number of subjects involved in the study (e.g., include when the research involves more than minimal risk).
- Use of a written translation of the entire IRB approved English consent form is required for subjects who do not speak English or understand English and where researchers can reasonably expect that more than an incidental number of subjects speaking the same non-English language will be enrolled (e.g., if the Investigator is targeting a non-English speaking group). The IRB must approve all translated versions of the consent form. The IRB recommends the translation is done by a certified translator, however, the IRB will consider, on a case-by-case basis, allowing other translators to perform this function with verification that the translation is an accurate and acceptable presentation of the entire English version. The IRB may have added requirements in the review process to assure the translation is accurate.
- A statement that the monitor, the auditor, the IRB, and the regulatory authority will be granted direct access to the participant's original medical records for verification of clinical trial procedures or data, without violating the confidentiality of the participant, to the extent permitted by the applicable laws and regulations and that, by signing a written consent form, the participant or the participant's legally acceptable representative is authorizing such access.
- The approval of the IRB.

- For research regulated by FDA:
    - A statement that informs the subject of the possibility that FDA may inspect the records.
    - For applicable clinical trials, the following statement notifying the subject that clinical trial information has been or will be submitted for inclusion in the clinical trial registry databank: “A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This website will not identify you. At most, the website will include a summary of the results. You can search this website at any time.”
    - Investigational New Drug Application (IND) submitted to FDA is not required to contain a copy of the consent document. For significant risk devices, the consent document is considered to be a part of the investigational plan in the application for an Investigational Device Exemption (IDE). Any substantive changes to the document made by an IRB must be submitted to the FDA (by the sponsor) for review and approval.
    - There is a statement noting the possibility that the FDA may inspect the records that will be provided to each participant.

Regulations & Guidance: DHHS 45 CFR 46.116(b);

5.6.1 GCP Additional Elements of Informed Consent to be applied, as appropriate: When following the ICH-GCP (E6) guideline, the IRB determines that the following consent disclosures are included:

- The participant's responsibilities.
- When applicable, the reasonably foreseeable risks or inconveniences to an embryo, fetus, or nursing infant.
- When there is no intended clinical benefit to the participant, the participant should be made aware of this.

Additional situational-specific elements that an informed consent should include are:

- The trial treatment(s) and the probability for random assignment to each treatment.
- The compensation and/or treatment available to the subject in the event of trial-related injury.
- The anticipated prorated payment, if any, to the subject for participating in the trial.
- The anticipated expenses, if any, to the subject for participating in the trial
- That records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available. If the results of the trial are published, the subject’s identity will remain confidential.

- The expected duration of the subject's participation in the trial.

Regulations & Guidance: DHHS 45 CFR 46.116(b); FDA 21 CFR 50.25(b)

5.7 Documentation of Informed Consent

The IRB will ensure that the consent will be appropriately documented according to legal requirements in accordance with, and to the extent required by 45 CFR 46.117, 21 CFR 50.27, the Good Clinical Practices and to the ethical principles in the Declaration of Helsinki.

- Except as provided in section 5.10, informed consent must be documented by the use of a written consent form approved by the IRB and personally signed and dated by the subject or the subject's legally authorized representative at the time of consent.
- In addition to signing the consent document, the subject or representative should enter the date of signature on the consent document to permit verification that consent was actually obtained before the subject began participation in the study.
- If the consent is obtained on the same day as the subject's involvement in the study begins, the subject's medical records/source documentation should document that consent was obtained prior to participation in the study.
- Prior to a participant's participation in the trial, the written consent document should be signed and personally dated by the person who conducted the informed consent discussion.
- Participants or participant's legally authorized representative will be given adequate time to read the consent document before it is signed.
- If a participant is unable to read or if a legally acceptable representative is unable to read, an impartial witness should be present during the entire informed consent discussion.
    - After the written consent document and any other written information to be provided to participants, is read and explained to the participant or the participant's legally acceptable representative, and after the participant or the participant's legally acceptable representative has orally consented to the participant's participation in the trial and, if capable of doing so, has signed and personally dated the consent document, the witness should sign and personally date the consent document.
    - By signing the consent document, the witness attests that the information in the consent document and any other written information was accurately explained to, and apparently understood by, the participant or the

participant's legally acceptable representative, and that consent was freely given by the participant or the participant's legally acceptable representative.

- A copy of the signed and dated consent document will be provided to the participant or the participant's legally acceptable representative, a copy placed on all of the appropriate records, and the original signed consent document should be retained in the study records.
- To allow the use of the long form of consent documentation, the IRB will determine the following:
    - The required and appropriate additional elements of disclosure are included in the consent process
    - The consent document embodies the basic and required additional elements of disclosure.
    - The required disclosure will be provided to each participant or a legally authorized representative in accordance with legal requirements.
    - Whether additional disclosures are required for inclusion in the consent process.
    - The participant or the participant's legally authorized representative will sign the consent document
    - A copy of the consent document will be given to the person signing the consent document.
    - The researcher will give either the participant or the representative adequate opportunity to read the consent document before it is signed.

At this time Pennington Biomedical Research Center does not permit the informed consent documentation use of a "short form".

5.8 Continued Use of Data Following Withdrawal or Termination

- When a participant withdraws from a study, the data collected on the participant to the point of withdrawal remains part of the study database and may not be removed. The consent document cannot give the participant the option of having data removed.
- A researcher may ask a participant who is withdrawing whether the participant wishes to provide continued follow-up and further data collection subsequent to their withdrawal from the interventional portion of the study. Under this circumstance, the discussion with the participant distinguishes between study-related interventions and continued follow-up of associated clinical outcome information, such as medical course or laboratory results obtained through non-invasive chart review, and address the maintenance of privacy and confidentiality of the participant's information.

- The researcher must obtain the participant's consent for this limited participation in the study (assuming such a situation was not described in the original consent document). The IRB must approve the consent document.
- If a participant withdraws from the interventional portion of a study and does not consent to continued follow-up of associated clinical outcome information, the researcher must not access for purposes related to the study the participant's medical record or other confidential records requiring the participant's consent. However, a researcher may review study data related to the participant collected prior to the participant's withdrawal from the study, and may consult public records, such as those establishing survival status.

5.8.1 FDA Regulated Studies

It is the FDA policy that participant data collected up to the time of withdrawal must remain in the data set in order for the study to be scientifically valid.

5.9 Consent Monitoring

In reviewing the adequacy of informed consent procedures for proposed research, the IRB may on occasion determine that special monitoring of the consent process by an impartial observer (consent monitor) is required in order to reduce the possibility of coercion and undue influence, ensure that the approved consent process is being followed, or ensure that subjects are truly giving informed consent.

Such monitoring may be particularly warranted for: high risk studies; studies that involve particularly complicated procedures or interventions; studies involving highly vulnerable populations (e.g., children); studies involving study staff with minimal risk experience in administering consent to potential study subjects, or other situations when the IRB has concerns that consent process is not being conducted appropriately.

Monitoring may also be appropriate as a corrective action where the IRB has identified problems associated with a particular Investigator or a research project.

If the IRB determines that consent monitoring is required, the HRPP Director will develop a monitoring plan and submit it to the IRB for approval. The consent monitoring may be conducted by HRPP Director, IRB staff, IRB members or another party, either affiliated or not with the institution. The investigator will be notified of the IRB determination and the reasons for the determination. Arrangements will be made with the investigator for the monitoring of the consent process for a specified number of subjects. When observing the consent process, the monitor will determine:

- Whether the informed consent process was appropriately completed and documented;
- Whether the subject had sufficient time to consider study participation;
- Whether the consent process involved coercion or undue influence;
- Whether the information was accurate and conveyed in understandable language; and
- Whether the subject appeared to understand the information and gave their voluntary consent.

Following the monitoring, a report of the findings will be submitted to the IRB, which will determine the appropriate action to be taken.

5.10 Waiver of the Consent Process

An IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth above; or waive the requirements to obtain informed consent, provided the IRB finds and documents that:

- The research involves no more than minimal risk tangible or intangible risk to the subjects;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects;
- The research could not practicably be carried out without the waiver or alteration; and whenever appropriate, the subjects must be provided with additional pertinent information after participation.
- If the research involves using identifiable private information or identifiable biospecimens, the research cannot practicably be carried out without using such information or biospecimens in an identifiable format.
- The IRB must determine the regulatory criteria for waivers or alterations of the consent process are met.
- The research is not regulated by the FDA.

In addition, an IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent; or waive the requirements to obtain informed consent, provided the IRB finds and documents that the research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:

- Public benefit or service programs;
- Procedures for obtaining benefits or services under those programs;
- Possible changes in or alternatives to those programs or procedures; or

- Possible changes in methods or levels of payment for benefits or services under those programs.
- The research is not FDA-regulated

Regulations & Guidance: DHHS 45 CFR 46.116(c)-(d); 117(c); FDA 21 CFR 50.23

5.10.1 FDA Waiver of the Consent Process

Waiver of informed consent for certain FDA-regulated minimal risk clinical investigations will facilitate investigators' ability to conduct studies that may contribute substantially to the development of products to diagnose or treat diseases or conditions, or address unmet medical needs. The IRB may approve a consent procedure that does not include, or that alters, some or all of the elements of informed consent set forth in 21 CFR 50.25, or waiving the requirements to obtain informed consent when the IRB finds and documents that:

1. The clinical investigation involves no more than minimal risk (as defined in 21 CFR 50.3(k) or 56.102(i)) to the subjects;
2. The waiver or alteration will not adversely affect the rights and welfare of the subjects;
3. The clinical investigation could not practicably be carried out without the waiver or alteration; and
4. Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

FDA does not intend to object to a sponsor initiating, or an investigator conducting, a minimal risk clinical investigation for which an IRB waives or alters the informed consent requirements as described above.

Regulations & Guidance: FDA 21 CFR 50.25, IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects

5.11 Waiver of Parental Permission

In some cases the IRB is allowed to waive parental permission by determining the criteria for waivers or alterations is met.

- Research on Public Benefit or Service Programs
    - The IRB can waive or alter the requirements for parental permission for non-exempt research examining state or local public benefit or service programs or certain features of those programs if all of the following criteria are met:

        - The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine public benefit or service programs, procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs
        - The research could not practicably be carried out without the waiver or alteration
        - The research is not FDA-regulated.

- Minimal Risk Research
    - The IRB can waive or alter the requirements for parental permission for non-exempt research that meets all of the following criteria:
        - The research involves no more than minimal risk to subjects.
        - The waiver or alteration will not adversely affect the rights and welfare of subjects.
        - The research could not practicably be carried out without the waiver or alteration.
        - Whenever appropriate, subjects will be provided with additional pertinent information after participation
        - The research is not FDA-regulated.

- Research Designed to Study Conditions in Children
    - The IRB can waive or alter the requirements for parental permission for non-exempt research designed to study conditions in children or a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (e.g., neglected or abused children) when the following additional criteria are also met:
        - An appropriate mechanism is in place to protect the children
        - The waiver is not inconsistent with federal, state, or local law.
        - The research is not FDA-regulated.
- Note: IRBs may waive the requirement for obtaining parental or guardian permission as described above even if the research involves greater than minimal risk to the participants. When determining an appropriate mechanism for protecting child participants (e.g., appointment of an advocate or assent monitor), investigators and IRBs will consider the nature of the research (including any potential risks and anticipated benefits) and the children's ages, maturity, condition, and psychological/emotional states.

5.12 Waiver of Documentation of Informed Consent

The IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either that the:

- Only record linking the subject and the research would be the consent document and the principle risk would be potential harm resulting from a breach of confidentiality; Subjects must be asked whether they want documentation linking them with the research, and their wishes must govern.
- The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. Procedures such as non-sensitive surveys, questionnaires and interviews generally do not require written consent when conducted by non-researchers.
- If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.
- For screening, recruiting, and determining eligibility, the researcher will obtain information through oral or written communication with the prospective participant or legally authorized representative, or
    - The researcher will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.
- In regards to confidentiality, the oral or written information provided to participants includes all required and appropriate additional elements of consent disclosure.
- For distinct cultural groups, the oral or written information provided to participants includes all required and appropriate additional elements of consent disclosure.

When following DHHS and FDA requirements:

- Waiver of Documentation of the Consent Process: Consent normally not required outside the research context
    - The oral or written information provided to participants includes all required and appropriate additional elements of consent disclosure.

In cases in which the documentation requirement is waived, the IRB requires the investigator to provide in the application materials a written summary of the information to be communicated to the subject; the IRB will consider whether to require the investigator to provide subjects with a written statement regarding the research.

The IRB Chair or primary reviewer will complete a review of the request for waiver of informed consent. In addition, the IRB minutes will document required determination regarding waiver of requirements for written documentation of informed consent. The minutes also will document the protocol specific findings justifying the requirements.

Consent form for clinical trials. Each clinical trial conducted or supported by a Federal department or agency must have an approved consent form, and this form must be posted online. (§ ____.116(h)). A “clinical trial” is a “research” study in which one or more “human subjects” are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health related outcomes? (§__.101(a)(2), §__.102(b)). This provision applies only to those clinical trials that are conducted or supported by a federal department or agency.

When following DHHS requirements:

- Consent form must be posted by the principal investigator of the study
    - After clinical trial is closed to recruitment, AND
    - no later than 60 days after the last study visit by any subject required by the protocol, AND
    - On a website specified by the U.S. Federal Government
- Sponsors or investigators of certain clinical trials are required by U.S. law to register their trials on and submit summary results to ClinicalTrials.gov.
- If the researcher wants to request an exception to the requirement to post the consent document and the process to redact confidential commercial information from the consent, they must follow guidance from the Federal agency.

6.0 Vulnerable Subjects in Research

6.1 Policy

The following procedures describe the requirements for involving vulnerable subjects in research under the purview of the Pennington Biomedical Research Center IRB.

6.2 Involvement of Vulnerable Populations

When some or all the subjects in a protocol are likely to be vulnerable to coercion or undue influence, the investigator should include additional safeguards to protect the rights and welfare of these subjects. Some of the vulnerable populations that might be involved in research include individuals who are children, pregnant women, fetuses, neonates or economically or educationally disadvantaged, adults who lack the ability to consent, students, employees or homeless persons.

Additional requirements for IRB oversight of research involving vulnerable subjects can be found at 45 CFR part 46, which includes the following: subpart B - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research; and subpart D - Additional Protections for Children Involved as Subjects in Research. Pennington Biomedical Research Center does not review research under Subpart C - Research Involving Prisoners.

DHHS-funded research that involves any of these populations must comply with the requirements of the relevant subparts. Research funded by other federal agencies may or may not be covered by the subparts.

Under Pennington Biomedical Research Center FWA, the subparts only apply to DHHS-funded research and research funded by another federal agency that requires compliance with the subparts (FDA regulations include Subpart D, which applies to all FDA-regulated research). The following policies and procedures, which are based on the subparts, apply to all research regardless of funding. The individual sections describe how the subparts apply to DHHS-funded research.

6.3 Definitions

Vulnerable population (or “vulnerable subjects”): This includes the following classes of potential or actual research subjects: children, pregnant women, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.

6.4 IRB Responsibilities

- The IRB reviews the investigator's justifications for including vulnerable populations in the research to assess appropriateness of the research proposal.
- The IRB must ensure that additional safeguards have been included in each study to protect the rights and welfare of vulnerable subjects as needed at the time of initial review of the research proposal.
- The IRB shall continue to review research at intervals appropriate to the degree of risk and determine whether the proposed research continues to fulfill criteria for approval. Information reviewed should include the number of subjects considered as members of specific vulnerable populations.
- The IRB needs to carefully review the DSMB plan for all research involving vulnerable subjects.
- The IRB should be knowledgeable about and experienced in working with populations who are vulnerable to coercion and undue influence. If the IRB requires additional qualification or expertise to review a protocol, it should obtain consultation.

6.5 Procedures

6.5.1 Initial Review of Research Proposal

The following steps are relevant with respect to initial review of a research proposal:

- The investigator is responsible for identifying the enrollment of potential vulnerable subjects in the research proposal and provide the justification for their inclusion in the study. The investigator is responsible for identifying patients who are at risk for impaired decisional capacity as a consequence of psychiatric illness, and who are being asked to participate in a research study with greater than minimal risk.
- The IRB evaluates the proposed plan for consent of the specific vulnerable populations involved. If the research involves adults unable to consent, the IRB evaluates the proposed plan for permission of legally authorized representatives.
- The IRB evaluates and approves the proposed plan for the assent of subjects.
- The IRB evaluates the research to determine the need for additional protections.
- The investigator should provide appropriate safeguards to protect the subject's rights and welfare, which may include the addition of an independent monitor. The independent monitor is a qualified individual not involved in the research study who will determine the subject's capacity to provide voluntary informed consent.

- The IRB assess the adequacy of additional protections for vulnerable populations provided by the investigator.

6.5.2 Continuing Review and Monitoring

At continuing review, the investigator should identify the number of vulnerable subjects enrolled and any that needed an independent monitor in the progress report.

6.6 Research Involving Pregnant Women or Fetuses

6.6.1 Definitions

Delivery: means complete separation of the fetus from the woman by expulsion, extraction, or any other means.

Fetus: is the product of conception from the time of implantation until delivery. [DHHS 45 CFR 46.202(c); LA R.S. 40:1061.9].

Pregnant: is the period of time from confirmation of implantation until expulsion or extraction of the fetus. [DHHS 45 CFR 46.202(f)].

6.6.2 Research Not Funded by DHHS

For research not funded by DHHS, no additional safeguards are required by the regulations and there are no restrictions on the involvement of pregnant women in research where the risk to the fetus is no more than minimal risk.

Pregnant women or fetuses may be involved in research not funded by DHHS involving more than minimal risk to fetuses if all of the following conditions are met:

- Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
- The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus;
- Any risk is the least possible for achieving the objects of the research;
- If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, then the consent of the pregnant woman is obtained in accordance with the provisions for informed consent;
- If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accordance

with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest;
- Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
- For children who are pregnant, assent and permission are obtained in accordance with the provisions of permission and assent (see section 6.8.3.2);
- No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
- Individuals engaged in the research will have no part in determining the viability of a neonate.

Regulations & Guidance: DHHS 45 CFR 46.204.

6.6.3 Research Funded by DHHS

For DHHS-funded research, 45 CFR subpart B applies to all research involving pregnant women. According to 45 CFR subpart B, pregnant women or fetuses may be involved in research funded by DHHS if all of the following conditions are met:

- Where scientifically appropriate, pre-clinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risk to pregnant women and fetuses.
- The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal risk and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
- Any risk is the least possible for achieving the objects of the research;
- If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal risk and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, then the consent of the pregnant woman is obtained in accordance with the provisions for informed consent.

- If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accordance with the provisions for informed consent, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
- Each individual providing consent is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
- For children who are pregnant, assent and permission are obtained in accord with the provisions of permission and assent in section 6.8.3.2;
- No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
- Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
- Individuals engaged in the research will have no part in determining the viability of a neonate.

6.7 Research Involving Neonates

6.7.1 Definitions

Neonate: means newborn. [DHHS 45 CFR 46.202(d)].

Neglect: neglect of neonate means a medical finding by a Louisiana licensed physician that a neonate either is dependent upon or suffers from withdrawal symptoms from an illegal controlled dangerous substance. It also includes a medical finding by a physician that a neonate suffers from an illness, disease or condition attributable to the exposure of the newborn, in utero, of an illegal CDS.

Non-Viable Neonate (or "Non-Viable Fetus"): is a fetus ex utero that, although living, is not able to survive to the point of independently maintaining a heartbeat and respiration. [DHHS CFR 46.202(e)].

Viable Neonate (or "Viable Fetus"): means a fetus that is able, after delivery, to survive to the point of being able to independently maintain a heartbeat and respiration (given the benefit of available medical therapy). [DHHS 45 CFR 102(c) & (l); 45 CFR 46.202(h)].

6.7.2 General Requirement Regarding Research Involving Neonates

Neonates of uncertain viability and non-viable neonates may be involved in research if all of the following conditions are met:

- Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates;
- Each individual that's providing consent is fully informed regarding the reasonably foreseeable impact of the research on the neonate; and
- Individuals engaged in the research will have no part in determining the viability of a neonate.

The requirements of neonates of uncertain viability or non-viable neonates (see below in this section) have been met as applicable.

Regulations & Guidance: DHHS 45 CFR 46.205(a).

6.7.3 Neonates of Uncertain Viability

Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this subpart unless the following additional conditions have been met.

The IRB determines that:

- The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective; or
- The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and
- The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accordance with the provisions of permission and assent, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.
- The IRB Chair will have the IRB determine and document individuals providing consent are fully informed regarding the reasonably foreseeable impact of the research on the neonate.

Regulations & Guidance: DHHS 45 CFR 46.205(b).

6.7.4 Non-Viable Neonates

After delivery, non-viable neonates may not be involved in research covered by this subpart unless all of the following additional conditions are met:

- Vital functions of the neonate will not be artificially maintained;
- The research will not terminate the heartbeat or respiration of the neonate;
- There will be no added risk to the neonate resulting from the research;
- The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and
- The legally effective informed consent of both parents of the neonate is obtained in accordance with the provisions of permission and assent, except that the waiver and alteration of the provisions of permission and assent do not apply.
- However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a non-viable neonate will suffice to meet the requirements of this paragraph, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a non-viable neonate will not suffice to meet the requirements of this paragraph.
- The IRB Chair will have the IRB determine and document individuals providing consent are fully informed regarding the reasonably foreseeable impact of the research on the neonate.

Regulations & Guidance: DHHS 45 CFR 46.205(c).

6.7.5 Viable Neonates

A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accordance with the requirements of IRB review process and research involving children. [DHHS 45 CFR 46.205(d)].

6.7.6 Research involving, After Delivery, the Placenta, the Dead Fetus or Fetal Material

Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, must be conducted only in accordance with any applicable federal, state, or local laws and regulations regarding such activities.

If information associated with material described above in this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research participants and all pertinent sections of this document are applicable. [DHHS 45 CFR 46.206].

6.7.7 Research Not Otherwise Approvable

6.7.7.1 Research Not Funded by DHHS

If the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and the research is not approvable under the above provisions, then the IRB will consult with a panel of experts in pertinent disciplines (e.g., science, medicine, ethics, and law). Based on the recommendation of the panel, the IRB may approve the research based on either:

- That the research in fact satisfies the conditions of Section 6.6, as applicable; or
- The following:
    - The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;
    - The research will be conducted in accordance with sound ethical principles; and
    - Informed consent will be obtained in accordance with the provisions for informed consent and other applicable sections of this document.

Regulations & Guidance: DHHS 45 CFR 46.207.

6.7.7.2 Research Funded by DHHS

DHHS-funded research that falls in this category must be approved by the Secretary of DHHS. If the IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and the research is not approvable under the above provisions, then the research will be sent to OHRP for DHHS review.

Newborns are only considered neonates until they are determined to be viable (able to survive outside of the uterus). Once they are determined to be viable, they are considered children; the IRB will follow guidelines from section 6.8 Research Involving Children.

6.8 Research Involving Children

The following applies to all research involving children, regardless of funding source. The requirements in this section are consistent with subpart D of 45 CFR 46 (applicable to DHHS-funded research) and subpart D of 21 CFR 50 (applies to FDA-regulated Research involving Children).

Regulations & Guidance: FDA 21 CFR 56.109(h); 21 CFR 56.111(c)].

6.8.1 Definitions

Assent: means a child's affirmative agreement to participate in research. Mere failure of a child to object may not, absent affirmative agreement, be construed as assent. [FDA 21 CFR 50.3(n)].

Child: are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. [DHHS 45 CFR 46.402(s); FDA 21 CFR 50.3(o)].

According to Louisiana Law, the legal age for consent for treatment or medical procedures is 18 years or older. [LA Children's Code 116; LA R.S. 40.1079.1]. Louisiana law is silent with respect to the legal age to consent with respect to research. For purposes of these SOPs, any person who is under the age of 18 generally is unable to consent for him/herself. Several important exceptions exist under Louisiana law that effectively treat children as adults and gives them the capacity to consent to their own medical care and to participate in research. They include the following: for a child to receive medical and/or surgical care at a hospital and/or to receive physicians' services [LA R.S. 40:1079.1]. This may or may not overlap with the proposed research; if a child is emancipated by marriage. Regardless of age, a child is fully emancipated upon his or her marriage [LA Civil Code Art 367]; if a child is judicially emancipated. This requires a court order for child older than 16 years of age [LA Civil Code Art 366 and 1922];

If a child is emancipated by authentic act this requires a child older than 16 years of age and the child's parents to execute a written document of emancipation, signed before two witnesses and a notary [LA Civil Code Art 368]; if a child seeks to be treated for venereal disease [LA R.S. 40:1121.8]; and if a child seeks to be treated for drug abuse [LA R.S. 40:1079.2].

Because Louisiana law does not specifically address consent of children with majority status to research, the institution's IRB will review issues of consent related to enrollment of these children in research on a case-by-case basis.

Guardian (or legal guardian): means an individual who is authorized under applicable state or local law to consent on behalf of a child to (a) general medical care when general medical care includes participation in research; or (b) to participate in research. [DHHS 45 CFR 46.402(e); FDA 21 CFR 50.3(s); LA. Children's Code 112 (5.1)]. A guardian of a minor retains the duty and authority to (1) act in the best interests of the minor, subject to residual parental rights and responsibilities (if any); (2) make important decisions in matters having a permanent effect on the life and development of the minor; and (3) to be concerned with the minor's general welfare. For research conducted in jurisdictions other than Louisiana, the research must comply with the laws regarding guardianship in all relevant jurisdictions where the research will take place.

Health Agent: is an authorized representative legally acting for a person pursuant to a Durable Power of Attorney for Health Care (Medical Power of Attorney) or other legal document permitted within a jurisdiction that allows a person to appoint another person(s) to make medical decisions for the patient if the patient should become temporarily or permanently unable to make those decisions for himself/herself. Any adult (18 or older) can be granted this power. [LA R.S.40:1159.4].

Legally Authorized Representative: is an individual, judicial, or other body authorized under applicable law to consent or otherwise provide permission on behalf of a subject, either prospectively or during the course of research, to the subject's participation in the procedure(s) involved in the research. [DHHS 45 CFR 46.102(c); FDA 21 CFR 50.3(l)]. For the purposes of this document, a legally authorized representative includes a person appointed as a health agent, a court-appointed legal guardian of the person, as well as next-of-kin in the following order of priority unless otherwise specified by applicable state law: the subject's spouse; adult child(ren) of subject (18 years of age or older); parent of subject; adult sibling(s) of subject (18 years of age or older); grandparent(s) of subject; or adult grandchild(ren) of subject (18 years of age or older). If there is more than one person within the above named class, the consent shall be given by a majority of those members of the class available for consultation. [LA R.S. 40:1159.4] legally authorized representative should not be confused with legal guardian.

Minor: means any person under the age of 18 years. [LA Civil Code Art 116]. Do not confuse the definitions of minor (pertaining to a person's age) with child/children (pertaining to a person's ability to assent).

Parent: means a child's biological or adoptive parent.

[FDA 21 CFR 50.3(p)].

6.8.2 Allowable Categories

Research on children must be reviewed and categorized by the IRB into one of the following groups:

1. Not greater than minimal risk: research on children not involving physical or emotional risk greater than that ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests (i.e., minimal risk). This includes adequate provisions are made for soliciting the assent of children and the permission of their parents or legal guardians as set forth in section 6.8.3.
2. Greater than minimal risk: research on children involving greater than minimal risk but presenting the prospect of direct benefit to the individual subject.
    - The risk is justified by the anticipated benefit to the subjects;
    - The relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches; and
    - Adequate provisions are made for soliciting the assent of children and the permission of their parents or legal guardians as set forth in section 6.8.3.
3. Greater than minimal risk and no prospect of direct benefit: research on children involving greater than minimal risk and no reasonable prospect of direct benefit to the individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.
    - The risk represents a minor increase over minimal risk;
    - The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
    - The intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance to the understanding of amelioration of the subjects' disorder or condition; and
    - Adequate provisions are made for soliciting the assent of children and the permission of their parents or legal guardians as set forth in section 6.8.3.
4. Research Not Otherwise Approvable: research on children not otherwise approvable which presents an opportunity to understand, prevent, or alleviate

serious problems affecting the health or welfare of children. Federally-funded research in this category must be approved by the DHHS Secretary, and requires consent of either both parents and the legal guardian. FDA-regulated research in this category must be approved by the FDA Commissioner. For non-federally funded research, the IRB Chair will consult with a panel of experts in pertinent disciplines (e.g., science, medicine, ethics, or law) and following opportunity for public review and comment, determine either:

- That the research in fact satisfies the conditions of the previous categories, as applicable; or
- The following:
    - The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children;
    - The research will be conducted in accordance with sound ethical principles; and
    - Informed consent will be obtained in accordance with the provisions for informed consent and other applicable sections of this document. Adequate provisions are made for soliciting the assent of children and the permission of their parents or legal guardians as set forth in section 6.8.3.

Regulations & Guidance: DHHS 45 CFR 46.404; 45 CFR 46.405; 45 CFR 46.406; 45 CFR 46.407.

6.8.3 Parental Permission and Assent

6.8.3.1 Parental Permission

Since a child cannot consent for him/herself, the IRB must determine that adequate provisions have been made for soliciting the permission of each child's parent or legal guardian, as documented in the consent (the sample minor document can be found at www.pbrc.edu/HRPP/Forms)

Consent should be obtained as follows in this order of priority: mother and father or adoptive foster parents [LA R.S. 40:1159.6]. The right first rests with married parents of the child. If they consent, comply with their wishes (subject to the assent requirements below). If they do not agree, the father's choice prevails. A power of attorney from the child's parents to another adult; The court recognized tutor [LA Civil Code Art 246]; or a power of attorney from the child's tutor to another adult [LA R.S. 9:951].

For research conducted in jurisdictions other than Louisiana, the research must comply with the laws regarding the legal age of consent in all relevant jurisdictions. The institution's legal department will provide assistance to the IRB office and investigators with regard to the laws in other jurisdictions.

Parents or legal guardians must be provided with the basic elements of consent and any additional elements the IRB deems necessary, as described in Policy 5.

In addition to the requirements under Louisiana law, the IRB may find that the permission of one parent is sufficient for research to be conducted under FDA categories CFR 21.51 or 50.52 45, or under HHS categories CFR 46.404 or 45 CFR 46.405. Consent from both parents is required for research to be conducted under categories CFR 21. 50.52 or 50.52, or under HHS categories 45 CFR 46.406 or 45 CFR 46.407 unless:

- One parent is deceased, unknown, incompetent, or not reasonably available; or
- When only one parent has legal responsibility for the care and custody of the child.

For research not covered by the FDA regulation, the IRB may waive the requirement for obtaining consent from a parent or legal guardian if: The research meets the provisions for waiver in Policy 5 or if the IRB determines that the research protocol is designed for conditions or a subject population for which parental or legal guardian permission is not a reasonable requirement to protect the subjects (e.g., neglected or abused children) provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and that the waiver is not inconsistent with federal, state or local laws. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

For research that involves no more than minimal risk or more than minimal risk with the prospect of direct benefit to the individual children, the IRB determines whether:

- The permission of both parents is required unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child, or the permission of one parent is sufficient.

- For research that involves more than minimal risk without the prospect of direct benefit to the individual children, the IRB determines that the permission of both parents is required unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

Parental permission may not be waived for research covered by the FDA regulations.

Permission from parents or legal guardians must be documented in accordance with and to the extent required by HRPP Policy 5.

Regulations & Guidance: DHHS 45 CFR 46.408

6.8.3.2 Assent from Children

Because assent means a child's affirmative agreement to participate in research, the child must actively show his or her willingness to participate in the research, rather than just complying with directions to participate and not resisting in any way. When judging whether children are capable of assent, the IRB is charged with taking into account the ages, maturity, and psychological state of the children involved.

The IRB should take into account the nature of the proposed research activity and the ages, maturity, and psychological state of the children involved when reviewing the proposed assent procedure and the form and content of the information conveyed to the prospective subjects. For research activities involving adolescents whose capacity to understand resembles that of adults, the assent procedure should likewise include information similar to what would be provided for informed consent by adults or for parental permission. For children whose age and maturity level limits their ability to fully comprehend the nature of the research activity but who are still capable of being consulted about participation in research, it may be appropriate to focus on conveying an accurate picture of what the actual experience of participation in research is likely to be (e.g., what the experience will be, how long it will take, whether it might involve any pain or discomfort). The assent procedure should reflect a reasonable effort to enable the child to understand, to the degree they are capable, what their participation in research would involve.

The IRB presumes that children ages 9 and older should be given an opportunity to provide assent. Generally, oral assent through the use of a script should be obtained from children 9 -11 years of age. Written assent using a written

document for the children to sign may be sought for older children. This opportunity can be extended to children at age 7, provided the child's age and maturity level enables the child to comprehend the nature of the research activity.

At times there may be inconsistency between parent permission and child assent. Usually a "no" from the child overrides a "yes" from a parent, but a child typically cannot decide to be in research over the objections of a parent. Obviously, there are individual exceptions to these guidelines (such as when the use of an experimental treatment for a life threatening disease is being considered). The general idea, however, is that children should not be forced to be research subjects, even when their parents' consent to it.

If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research.

The IRB will determine and document that assent is a requirement of: all children, some children or none of the children. When the IRB determines that assent is not a requirement of some children, the IRB determines and documents which children are not required to assent.

6.8.3.2.1 Determination by the IRB Assent is not a Requirement

When the IRB determines that assent is not a requirement for some or all children, the IRB determines and documents one or more of the following:

- The children are not capable of providing assent based on the age, maturity, or psychological state.
- The capability of the children is so limited that they cannot reasonably be consulted.
- The intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the child and is available only in the context of the research.
- Assent can be waived using the criteria for waiver of the consent process.

6.8.3.2.2 Determination by the IRB Assent is a Requirement

When the IRB determines that assent is a requirement, the IRB determines whether:

- Assent will be documented.
- If so, the process to document assent.

Even when the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances detailed in the Waiver of Informed Consent section of Policy 5.

Regulations & Guidance: DHHS 45 CFR 46.408.

6.8.3.3 Consent from Pregnant Minors

A minor may consent to medical care or the administration of medication by a hospital licensed to provide hospital services or by a physician licensed to practice medicine for the purpose of alleviating or reducing pain, discomfort, or distress of and during labor and childbirth. [LA R.S. 40:1079.1]. This consent shall be valid and binding as if the minor had achieved her majority, and it shall not be subject to a later disaffirmance by reason of her minority.

If research pertains to such permitted minor consent, then the minor may consent to the involved research. If not and the IRB has not waived the consent requirement, then assent from the minor is required, as well as parental permission.

6.8.4 Assent Form

When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

Researchers should try to draft a form that is age appropriate and study specific, taking into account the typical child's experience and level of understanding, and composing a document that treats the child respectfully and conveys the essential information about the study. The assent form (Sample Child’s Assent on the HRPP website) should:

- Tell why the research is being conducted;
- Describe what will happen and for how long or how often;
- Say it's up to the child to participate and that it is permissible to say no;
- Explain if it will hurt and if so for how long and how often;
- Say what the child's other choices are;

- Describe any good things that might happen;
- Say whether there is any compensation for participating; and
- Ask for questions.

For younger children, the document should be limited to one page if possible. Illustrations might be helpful, and larger type makes a form easier for young children to read. Studies involving older children or adolescents should include more information and may use more complex language.

6.8.5 Children who are Wards of the State

Children who are wards of the state or any other agency, institution, or entity can be included in research involving greater than minimal risk where there is no prospect of direct benefits to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition, only if such research is:

- Related to their status as wards; or
- Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

If the research meets the condition(s) above, the IRB Chair will determine an advocate must be appointed by the IRB or institution for each child who is a ward (one individual may serve as advocate for more than one child), in addition to any other individual acting on behalf of the child as legal guardian or *in loco parents*.

The advocate must be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

Regulations & Guidance: DHHS 45 CFR 46.409.

6.9 Persons with Impaired Decision Making Capacity

The requirements in this section apply to all research involving persons with mental disabilities or persons with impaired decision-making capacity regardless of funding source.

Research involving persons with impaired decision-making capability may only be approved when the following conditions apply:

- Only incompetent persons or persons with impaired decision making capacity (as determined by licensed health care professionals who are qualified to make such determinations consistent with the scope of their license) are suitable as research subjects. Competent persons are not suitable for the proposed research. The investigator must demonstrate to the IRB that there is a compelling reason to include incompetent individuals or persons with impaired decision-making capacity as subjects. Incompetent persons or persons with impaired decision-making capacity must not be subjects in research simply because they are readily available.
- The proposed research entails no significant risks, tangible or intangible, or if the research presents some probability of harm, there must be at least a greater probability of direct benefit to the subject. Incompetent people or persons with impaired decision-making capacity are not to be subjects of research that imposes a risk of injury, unless that research is intended to benefit that subject and the probability of benefit is greater than the probability of harm.
- Procedures have been devised to ensure that subject's representatives are well informed regarding their roles and obligations to protect incompetent subjects or persons with impaired decision making capacity. Health agents (appointed under Medical Power of Attorney) and next-of-kin, or legal guardians, must be given descriptions of both proposed research studies and the obligations of the person's representatives. They must be told that their obligation is to try to determine what the subject would do if competent, or if the subject's wishes cannot be determined, what they think is in the incompetent person's best interest. In addition and as appropriate, if assent can be obtained by a subject/potential subject with diminished decision making capacity (versus impaired), then the investigator should obtain such assent. The determination as to whether an individual retains capacity to assent must be determined by a duly qualified health care provider, consistent with the provider's scope of licensure.
- A non-therapeutic clinical trial (i.e., a trial in which there is no anticipated direct clinical benefit to the subject) should be conducted in subjects who personally give consent and who sign and date the written consent document. Non-therapeutic clinical trials may be conducted in subjects with consent of a legally authorized representative provided the following conditions are fulfilled:
    - The objectives of the trial cannot be met by means of a trial in subjects who can give consent personally;
    - The foreseeable risks to the subjects are low;
    - The negative impact on the subject's well-being is minimized and low.
    - The trial is not prohibited by law;
    - The opinion of the IRB is expressly sought on the inclusion of such subjects, and the written opinion covers this aspect; and

- Unless an exception is justified, the trial should be conducted in patients having a disease or condition for which the investigational product is intended. Subjects in such trials should be particularly closely monitored and should be withdrawn if they appear to be unduly distressed.

6.9.1 IRB composition

The IRB membership must include at least one member who is an expert in the area of the research. Consideration may be given to adding another member who is a member of the population, a family member of such a person or a representative of an advocacy group for that population. The IRB may utilize ad hoc members as necessary to ensure appropriate scientific expertise.

6.9.2 Determination of Decision-Making Capacity

The decision-making capacity of a potential research subject should be evaluated when there are reasons to believe that the subject may not be capable of making voluntary and informed decisions about research participation.

The investigator and research staff must have adequate procedures in place for assessing and ensuring subjects' capacity, understanding, and informed consent or assent. The IRB will evaluate whether the proposed plan to assess capacity to consent is adequate.

For research protocols that involve subjects with mental disorders that may affect decision-making capacity, the IRB may determine that capacity assessments are necessary, unless the investigator can justify why such assessments would be unnecessary for a particular group.

For research that poses greater than minimal risk, the IRB may require investigators to use independent and qualified professionals to assess whether potential subjects have the capacity to give voluntary, informed consent. Even in research involving only minimal risk, the IRB may require that the study include a capacity assessment if there are reasons to believe that potential subjects' capacity may be impaired. It is not necessary to require a formal capacity assessment by an independent professional for all potential research subjects with mental disorders. See the next section for details with respect to determining capacity to consent.

For research protocols involving subjects who have fluctuating or limited decision making capacity the IRB may ensure that Investigators establish and maintain ongoing communication with involved caregivers. Periodic re-consent should be considered in some cases. Third party consent monitors may be used during the recruitment and consenting process, or waiting periods may be required to allow more time for the

subject to consider the information that has been presented. For subjects with fluctuating decision making capacity or those with decreasing capacity to give consent, a re-consenting process with health agent may be necessary.

It is often possible for Investigators and others to enable persons with some decisional impairment to make voluntary and informed decisions to consent or refuse participation in research. Potential measures include repetitive teaching, group sessions, audiovisual presentations, and oral or written recall tests. Other measures might include follow-up questions to assess subject understanding, videotaping or audio-taping of consent interviews, second opinions, use of independent consent observers, interpreter for hearing-impaired subjects, allowing a waiting period before enrollment, or involvement of a trusted family member or friend in the disclosure and decision making process.

Although incompetent to provide informed consent, some persons may resist participating in a research protocol approved by their representatives. Under no circumstances may subjects be forced or coerced to participate.

In the event research subjects become incompetent or impaired in decision making capacity after enrollment, the investigator is responsible for notifying IRB staff. The investigator is responsible for developing a monitoring plan which follows the guidelines outlined above for incompetent and impaired decision making research subjects.

6.9.3 Determining Capacity to Consent

The majority of studies conducted at the institution only allow enrolling subjects who have the capacity to consent. For studies that have been approved for enrolling vulnerable populations who may lack capacity to consent, there must be someone who is able to assess capacity of each potential subject to consent. The investigator may determine after appropriate medical evaluation that the prospective research subject lacks decision-making capacity and is unlikely to regain it within a reasonable period of time. Additionally, if the reason for lack of capacity is because of mental illness then a psychiatrist or licensed psychologist must confirm this judgment and document in the individual’s medical record in a signed and dated progress note.

Decisional capacity in the research context has been interpreted by the American Psychiatric Association as requiring: ability to evidence a choice; ability to understand relevant information; ability to appreciate the situation and its likely consequences; and ability to manipulate information rationally.

A range of professionals and methods may be utilized to assess capacity. In general the consent assessor should be a researcher or consultant familiar with dementias and qualified to assess and monitor capacity and consent in such subjects on an ongoing basis. The IRB will consider the qualifications of the proposed individual(s) and whether he or she is sufficiently independent of the research team and/or institution.

A person who has been determined to lack capacity to consent to participate in a research study must be notified of that determination before permission may be sought from his or her legally authorized representative to enroll that person in the study. If permission is given to enroll such a person in the study, the potential subject must then be notified. If a person objects to participating, this objection should be respected.

6.9.4 Informed Consent and Assent

Whenever the subjects have the capacity to give consent (as determined by licensed health care professionals who are qualified to make such determinations consistent with the scope of their license), informed consent should be obtained and documented in accordance with Policy 5. When subjects lack the capacity to give consent, investigators may obtain consent from the legally authorized representative of a subject as described below.

A person who is incompetent or has been determined to lack capacity to consent to participate in a research study should be informed about the trial to the extent compatible with the subject's understanding and, if possible, the subject should give their assent to participate, sign and date the written informed consent or a separate assent form. If the person objects to participating, this objection should be heeded.

Both investigators and IRB members must be aware that for some subjects, their decision-making capacity may fluctuate. For subjects with fluctuating decision making capacity or those with decreasing capacity to give consent, a re-consenting process with legally authorized representative may be necessary. Although incompetent to provide informed consent, some persons may resist participating in a research protocol approved by their representatives. Under no circumstances may subjects be forced or coerced to participate.

6.9.5 Consent by Legally Authorized Representative

The regulations generally require that the investigator obtain informed consent from subjects. Under appropriate conditions, investigators also may obtain informed consent from a legally authorized representative of a subject (legally authorized representative).

This policy is designed to protect human subjects from exploitation and harm and, at the same time, make it possible to conduct essential research on problems that are unique to persons who are incompetent, or who have an impaired decision-making capacity.

Legally authorized representative may be obtained from a court appointed legal guardian of the person or a health agent appointed by the person in a Medical Power of Attorney. For example, a subject might have designated an individual to provide consent with regard to health care decisions through a durable power of attorney and have specified that the individual also has the power to make decisions on entry into research.

7.0 Drugs and Devices in Research

7.1 Drug Policy

All drugs, agents and/or biologics used in human subjects research under the purview of Pennington Biomedical Research Center IRB shall be stored, handled, and dispensed in compliance with regulations or requirements of the FDA, the Louisiana Board of Pharmacy (LABP), federal, state and other laws and regulations, and the policies and procedures of the HRPP. Furthermore, if research is conducted on Pennington Biomedical Research Center premises, such research shall be conducted in accordance with applicable institution and medical staff polices and guidelines.

All drugs, agents and/or biologics used in human subjects research requires approval from government regulatory agencies to use investigational drugs and devices in research. For organizations in the US, this means complying with requirements of the US FDA. For organizations outside the US, the approval to use investigational drugs and devices comes from the relevant authority in that country.

Pennington Biomedical Research Center Pharmacy provides administrative and clinical services to Investigators and research staff involved in drug-related research conducted at Pennington Biomedical facility under the purview of Pennington Biomedical Research Center's IRB. Furthermore, a Pennington Biomedical research pharmacist may be consulted by the IRB to have complete information about all IRB approved research that takes place at the facility.

Regardless of whether Investigators conduct drug studies for inpatients or outpatients, the institution's policy requires that the IRB review and approve all drug research involving human subjects prior to initiation of the study and prior to enrollment of subjects. When an IND is required by regulation or by IRB determination, the IRB staff ensures that research involving an investigational drug does not commence until a valid IND is in place. This includes recruiting, obtaining consent and screening participants for a specific study that is subject to the IND.

In general, the IND regulations in part 312 require that human research studies be conducted under an IND if **all** of the following conditions exist:

- The research involves a drug as that term is defined in section 201(g)(1) of the Federal Food, Drug, and Cosmetic Act (the FD&C Act) (21 U.S.C. 321(g)(1)).
- The research is a clinical investigation as defined in the IND regulations (21 CFR 312.3).
- The clinical investigation is not otherwise exempt from the IND requirements in part 312.

If the investigational drug requires an IND, the IRB staff will verify the IND number by requiring the sponsor's protocol or the FDA correspondence. The pharmacist will review any study that involves an investigational drug.

If the IRB determines that an IND is needed, the Investigator/sponsor must submit an IND application to the FDA and provide documentation of the outcome of the FDA determination (IND number) to the IRB before the IRB gives approval to enroll subjects in the study.

When the IRB determines that an IND may be required, the Investigator/sponsor must consult with the FDA. See FDA Guidance for Industry: Investigational New Drug Applications (INDs) - Determining Whether Human Research Studies Can Be Conducted Without an IND, Section VIII. Process for Addressing Inquiries Concerning the Application of IND Requirements.

If the FDA determines that the IND is exempt, the Investigator will receive a letter to that effect which must be uploaded into IRB Manager. If the FDA requires an IND application, all documentation from the FDA and from the sponsor/Investigator of the IND must be uploaded into IRB Manager.

Regulations & Guidelines: FDA 21 CFR 11; 21 CFR 54; 21 CFR 210; 21 CFR 211; 21 CFR 312; 21 CFR 314; 21 CFR320; 21 CFR 330; 21 CFR 601; 21 CFR 807; 21 CFR 812; 21 CFR 814; 21 CFR 820; 21 CFR 860

7.2 Definitions

***Administer*:** Means the direct application of a drug to the body of a research subject by injecting, inhalation, ingestion, or any other means. (LA R.S. 37:1164).

***Agents*:** are chemical agents that affect the function of living things.

***Biologic*:** a substance made from a living organism or its products and used in the prevention, diagnosis, or treatment of certain health conditions.

***Biological Products*:** are subsets of drugs used for the treatment, prevention or cure of disease in humans. FDA regulations and policies have established that biological products include blood-derived products, vaccines, in vivo diagnostic allergenic products, immunoglobulin products, products containing cells or microorganisms, and most protein products. Biological products, like other drugs, can be studied in clinical trials involving humans subjects under an IND in accordance with the regulations at 21 CFR 312.

***Clinical Investigation*:** means any experiment that involves a test article and one or more human subjects and that either is subject to requirements for prior submission to

the FDA under section 505 of the Federal Food, Drug, and Cosmetic Act the FDA Act) (21 U.S.C. 355) or to, or held for inspection by the Food and Drug Administration FDA) as part of an application for a research or marketing permit. (21 CFR 50.3)

Dietary Supplement: is defined by Dietary Supplement Health and Education Act of 1994 (DSHEA), as a product (other than tobacco) intended to supplement the diet that bears or contains one or more dietary ingredients. The dietary ingredients in these products can include vitamins, minerals, herbs and other botanicals, amino acids, other dietary substances intended to supplement the diet, and concentrates, metabolites, constituents, extracts, or combinations of the preceding types of ingredients. Dietary supplements are taken by mouth and can be found in many forms such as tablets, capsules, softgels, liquids, gelcaps, or powders.

- When a lawfully marketed dietary supplement is being studied for its effects on **diseases** (i.e., to cure, treat, mitigate, prevent, or diagnose **disease** including its associated symptoms) it is an investigational new drug and is subject to the 21 CFR 312 IND requirements. However, Investigators may request an exemption from 21 CFR 312 directly from the FDA.
- When a lawfully marketed dietary supplement is being studied for its dietary supplement use (i.e., structure and/or function claims), it is not an investigational new drug and is not subject to the 21 CFR 312 IND requirements. Structure and function claims are statements that describe the effect a dietary supplement may have on the structure or function of the human body.

***Dispense*:** means the interpretation, evaluation, and implementation of a prescription drug order, including the preparation and delivery of a drug or device to a patient or patient's agent in a suitable container appropriately labeled for subsequent administration to, or use by, a patient. Dispense necessarily includes a transfer of possession of a drug or device to the patient or the patient's agent. (LA R.S. 37:1164). Louisiana law requires that dispensing may only be done by a licensed pharmacist or a physician who is registered with the board as a dispensing physician. (LA R.S. 37:1201).

***Distribute or Distribution*:** means the delivery of a drug or device other than by administering or dispensing.

***Drug*:** means: a) any substance recognized in the official compendium, or supplement thereto, designated by the Louisiana Board of Pharmacy or other appropriate jurisdiction) for use in the diagnosis, cure, mitigation, treatment or prevention of diseases in humans, b) any substance intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in humans, or c) any substance other

than food intended to affect the structure or any function of the body of humans. (LA-R.S. 37:1164).

GRAS: refers to a product containing substances generally recognized as safe. Substances designated as GRAS for use in food are generally not approved as drug products. A clinical investigation of a GRAS substance that is intended to evaluate the product's ability to diagnose, cure, mitigate, treat, or prevent disease requires an IND under part 312, unless the substance to be studied is also a lawfully marketed drug and the clinical investigation meets the criteria for exemption under 21 CFR 312.2(b).

FDA Guidance for Clinical Investigators, Sponsors, and IRB: Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can Be Conducted Without an IND

***Investigational Drug*:** means a new drug or biological that is used in research. It also includes a biologic used *in vitro* for diagnostic purposes. The FDA considers the term investigational new drug or investigational drug to be synonymous with investigational drug (FDA 21 CFR 312.2). However, for purposes of this document, an investigational drug includes the following:

- An approved drug that is being studied for an unapproved or approved use in a controlled, randomized or blinded clinical trial.
- Those new drugs for which the Investigator or a sponsor has filed an IND application (FDA 21 CFR 312) which are exempt from pre-marketing approval requirements and may be lawfully shipped for use in clinical investigations in human subjects.

A drug that is lawfully marketed in the U.S. that may still be considered investigational and required that an IND be filed if the proposed use of such a drug involves a controlled study aimed towards seeking a significant change in labeling, advertising, route of administration, dosage level, dose regimen, or other factor that affects the risks associated with the use of the product (FDA 21 CFR 312.3 (b). The clinical investigation of a drug product that is not lawfully marketed in the United States requires submission of an Investigational New Drug (IND) Application to the FDA, unless exempt according to 21 CFR 312.2.

***Investigational New Drug Application or "IND"*:** refers to either an investigational new drug application or to a new drug that is used in clinical investigations. IND is synonymous with Notice of Claimed Investigational Exemption for a New Drug (FDA 21 CFR 312).

Off-Label Use: means the use of an approved drug, an approved or cleared device, or a licensed biologic for an indication not in the approved labeling. In general, research involving off-label use requires an IND or IDE (Investigational Device Exemption, if using a device) application.

Regulations & Guidelines: FDA "Off-Label and Investigational Use of Marketed Drugs, Biologics, and Medical Devices – Information Sheet

***Test Article*:** Is any drug including a biological for human use), medical device for human use, human additive, color additive, electronic product, or any other article subject to FDA regulation (FDA 21 CFR 50.3(j); 21 CFR 56.102 (l)).

7.3 FDA Exemptions

The following categories of clinical investigations are exempt from the requirements of FDA regulations for IRB review:

> Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the FDA or approved by the EPA or the Food Safety and Inspection Service of the U.S. DOA (FDA 21 CFR 56.104 (d)).

7.4 IND Requirements

The Investigator must indicate on the initial IRB application whether the research involves investigational drugs. If so, the Investigator must indicate if there is an IND for the research and provide documented assurance from the sponsor that the manufacture and formulation of investigational or unlicensed test articles conform to federal regulations. Documentation of the IND could be:

- Industry sponsored protocol with IND.
- Letter from FDA.
- Letter from industry sponsor.

If the research involves drugs and there is no IND, the Investigator must provide a rationale why it is not required.

The IRB staff or the IRB will determine:

- Whether there is an IND and if so, whether there is appropriate supporting documentation.

- If the research involves drugs or devices with no IND, and whether the research meets the criteria below.

7.4.1 IND Exemption

In general, Investigational New Drug (IND) regulations (21CFR312) apply in human research studies that involve use of a drug (as defined in the Food, Drug, and Cosmetic

Act (FD&C Act)) in a clinical investigation (as defined in 21CFR312.3) unless otherwise exempt from IND requirements.

Clinical investigations of lawfully marketed drug or biologic are exempt from IND requirements if **all** of the six criteria below are met:

i. it is not intended to be reported to FDA in support of a new indication for use or to support any other significant change in the labeling for the drug;
ii. it is not intended to support a significant change in the advertising for the product;
iii. it does not involve a route of administration or dosage level, use in a subject population, or other factor that significantly increases the risks (or decreases the acceptability of the risks) associated with the use of the drug product;
iv. it is conducted in compliance with the requirements for IRB review and informed consent [21 CFR parts 56 and 50, respectively];
v. it is conducted in compliance with the requirements concerning the promotion and sale of drugs [21 CFR 312.7]; and
vi. it does not intend to invoke 21 CFR 50.24.

The three most commonly occurring scenarios when clinical investigations may be exempted from the IND application requirements refer to:

1. certain limited situations of clinical investigations with approved marketed drugs;
2. bioavailability or bioequivalence studies; and
3. clinical investigations involving radioactive drugs considered safe for certain research uses.

For each of these and few other scenarios, the specific criteria for exemption must be met (21 CFR 312.2(b).

The following are also exempt from the IND requirements: a) a clinical investigation involving use of a placebo if the investigation does not otherwise require submission

of an IND; and b) a drug intended solely for tests in vitro or in laboratory research animals if shipped in accordance with 21 CFR 312.160.

For clinical investigations involving an in vitro diagnostic biological product, an IND is not necessary if:

- It involves one or more of the following: a) Blood grouping serum, b) Reagent red blood cells or c) Anti-human globulin;
- It is intended to be used in a diagnostic procedure that confirms the diagnosis made by another, medically established, diagnostic product or procedure; and
- It is shipped in compliance with 21 CFR 312.160.

Regulations & Guidelines: FDA Guidance for Clinical Investigators, Sponsors, and IRB: Investigational New Drug Applications (INDs) – Determining Whether Human Research Studies Can Be Conducted Without an IND

7.4.2 Responsibilities

This section describes the responsibilities and related responsibilities for handling investigational drugs or unlicensed test articles with respect to pharmacy, inventory control, reporting and documentation.

Regulations & Guidelines: FDA 21 CFR 312.61; 21 CFR 312.62; 21 CFR 312.69

7.4.2.1 Investigator Responsibilities - IND Determination

The Investigator is responsible for submitting sufficient information to the IRB to ensure proper IND determination. Required information may include, but is not limited to the following:

- Investigator's Brochure
- Package insert
- Summary of prior use/investigations
- FDA correspondence
- Plan for receipt, storage, control, labeling, and dispensing of drug
- A copy of any available supporting documentation (e.g., letter from the sponsor or FDA, other basis for determination) supporting claim that an IND is not required.

7.4.2.2 Investigator Responsibilities - Control of the Investigational Drug

An Investigator conducting a clinical investigation under an IND application is responsible for ensuring that the investigation is conducted according to the signed Investigator's statement Form 1572, the investigational plan, and the applicable Investigator's and sponsor's responsibilities including provisions for disqualification of clinical Investigators (21CRF 312.50-312.70). In addition, an Investigator is responsible for ensuring that the research is conducted according to Pennington Biomedical policies and procedures and must protect the rights, safety, and welfare of subjects under the Investigator's care and the control of drugs under investigation.

For Pennington Biomedical Research Center inpatients and outpatients, investigational drugs for research studies must be dispensed by the Pennington Biomedical research pharmacy. If a licensed Investigator by the Louisiana Board of Pharmacy requests to have control of the investigational drug agent or biologic then the Investigator must submit for IRB approval a plan for the distribution, storage, dispensing, accountability and destruction or return of drug at completion of the study for the investigational drug products.

An Investigator is expected to administer the drug only to subjects under the Investigator's personal supervision or under the supervision of a subordinate research staff responsible to the Investigator. The Investigator must not supply the investigational drug to any person not authorized to receive it. The investigator, or a person designated by the investigator/institution, should explain the correct use of the investigational product(s) to each subject and should check, at intervals appropriate for the trial, that each subject is following the instructions properly.

Where allowed/required, the investigator/institution may/should assign some or all of the investigator's/institution's duties for investigational product(s) accountability at the trial site(s) to an appropriate pharmacist or another appropriate individual who is under the supervision of the investigator/institution.

- **Dispensing to inpatients:** For participants in the inpatient unit of Pennington Biomedical Research Center, the Investigator must use the research pharmacy as the coordinating and control center for the research drug. As the coordinating and control center, the research pharmacy assumes the responsibility for maintaining records of the drugs delivered to the research pharmacy, inventory of the drug, dispensing of drugs to research subjects, and then return to the sponsor or disposition of unused product. The Pennington Biomedical research pharmacy will store and dispense the

investigational drug as specified by the sponsor and in accordance with applicable regulatory requirements.

Pennington Biomedical' s research pharmacy may initiate or adjust drug therapy and/or order laboratory tests associated with a research protocol when requested to do so by the Investigator. Any pharmacist participating in such a protocol must be trained and deemed competent to participate by the Investigator or his/her designee). Specific details on the adjustment of drug therapy or ordering of laboratory tests should be reviewed during the protocol initiation visit.

When Pennington Biomedical research pharmacy is the coordinating and control center for the research drug, the research pharmacy will store the returned dispensed investigational drug in a designated return area when a study protocol requires the subject to return the empty investigational drug container or any amount of the unused investigational drug. However, it is the responsibility of the Investigator or Investigator staff to deliver the returned dispensed investigational drug to research pharmacy when subjects leave the dispensed investigational drug in the outpatient clinic.

In coordinating the control of the research drug, the Investigator will forward a copy of the complete research protocol, a copy of the Investigator's drug brochure, research pharmacy manual, ordering procedures, any special storage, handling or preparation requirements, and any pertinent dispensing information to the research pharmacist.

A cost estimate should be obtained from research pharmacy during the initial stages of budget development. A pharmacy fee will be applied to all research involving investigational drugs. The research pharmacy will prepare a cost estimate of pharmacy fees after review of the above material.

- **Dispensing Controlled Substances:** controlled substances must be securely stored and must be dispensed by a duly licensed pharmacist.

- **Dispensing to Outpatients:** If a licensed Investigator by the Louisiana Board of Pharmacy requests to have control of the investigational drug agent or biologic then the Investigator must submit for IRB approval a plan for the distribution, storage, dispensing, accountability and destruction or return of drug at completion of the study for the investigational drug products.

    - **Drug Accountability Record -** The Investigator must maintain records of the product's delivery to the study site, the inventory at the site, the use by

each subject, and the return to the sponsor or alternative disposition of unused product. These records should include dates, quantities, batch/serial numbers, expiration dates, and the unique code numbers assigned to the investigational products and trial subjects. The Investigator should maintain records that document adequately that the subjects will provide the doses specified by the protocol and reconcile all investigational products received from the sponsor. The investigational drug supply is subject to audit by the IRB.

In regard to the use by each subject, Investigators should maintain drug accountability records that document adequately which subjects received the drug; when the subjects received the drug; the specific dosage the subjects received; and any returned amount of the dispensed investigational drug.

- **Drug Storage -** Investigational products should be stored as specified by the Sponsor and in accordance with applicable regulatory requirements. Storage guidelines, include:

  - Storage area is large enough for the supply of study drug.
  - Storage area can be locked.
  - Investigational drug is stored separately from other compounds.
  - Non-dispensed drug is stored separately from returned dispensed drug.
    - If the study protocol requires the subject to return the empty investigational drug container or any amount of the unused investigational drug, it is the Investigators responsibility to store the returned dispensed Investigational drug separately from the non-dispensed investigational drug.
    - It is the responsibility of the Investigator to deliver the returned dispensed investigational drug to the research pharmacy if it is the coordinating and control center for the research drug.
  - Inventory control procedures are used.
  - Any environmental controls are maintained.
  - Access is limited to study staff.
  - Controlled substances are not allowed to be stored outside Pennington Biomedical Research Center research pharmacy.

- **Drug Labeling for Investigational Drugs -** The following labeling requirements are required for investigational new drugs:

- The immediate package of an investigational new drug intended for human use shall bear a label with the statement, *Caution: New Drug – Limited by Federal or U.S. law* to investigational use (FDA 21 CFR 312.6).
- The label or labeling of an investigational new drug shall not bear any statement that is false or misleading in any particular way and shall not represent that the investigational new drug is safe or effective for the purposes for which it is being investigated (FDA 21 CFR 312.6).
- Participant Identifier
- Protocol number or name
- Strength of drug
- Dose
- Directions for use or administration
- Quantity dispensed

- **Drug Labeling for Drugs**: Louisiana rules and Pennington Biomedical Research Center require that all drugs dispensed shall contain a medication label with the following:

  - Pharmacy name, address and phone number
  - Prescription number
  - Name of prescriber
  - Patient's name
  - Date dispensed
  - Drug name and strength
  - Directions for use or administration
  - Pharmacist's name or initials
  - Auxiliary labels, if applicable
  - Indication that it is an investigational drug, if applicable

- **Drug Administration** – Investigational drugs shall be administered in accordance with any applicable federal or state laws and regulations and in accordance with any policies or procedures set forth by Pennington Biomedical Research Center. An informed consent document signed and dated by the subject and the Investigator must be in place before administering the drug.

  A person licensed within State of Louisiana and so authorized by their professional scope of practice shall administer an investigational drug to a subject. An Investigator may designate the responsibility of administering the drug only after the designee has been given and has demonstrated an understanding of basic information about the drug according to the

protocol. This education and delegation of responsibility must be documented.

Regulations & Guidelines: FDA 21 CFR 312.61

- The Investigator shall report all unanticipated problem involving risks to subjects or others to the IRB according to the procedures outlined in section 8 and all protocol violations and protocol deviations see section 9.0 (FDA 21 CFR 312.64). For research involving investigational new drugs:
  - The Investigator is required to inform research pharmacy that the IRB has approved the protocol through submission of the IRB approval letters.
  - The Investigator must inform the IRB and pharmacy when a study involving investigational drugs has been terminated by the sponsor.
  - The Investigator will report to the sponsor any adverse effect that may reasonably be regarded as caused by, or probably caused by, the drug (21 CFR 312 (b)) according to the procedures in the protocol.
  - The Investigator will insure the investigational products are manufactured, handled and stored in accordance with applicable good manufacturing practice.
  - Where allowed or required, the Investigator may assign some or all duties for investigational articles accountability at the trial sites to an appropriate pharmacist or another appropriate individual who is under the supervision of the Investigator.
  - The Investigator, pharmacist, or other designated individual will maintain records of the product's delivery to the trial site, the inventory at the site, the use by each participant, and the return to the sponsor or alternative disposition of unused products. These records will include dates, quantities, batch/serial numbers, expiration dates (if applicable), and the unique code numbers assigned to the investigational products and trial participants.
  - Investigators should maintain records that document adequately that the participants are provided the doses specified by the protocol and reconcile all investigational products received from the sponsor.
  - The Investigator will maintain the following:
    - Current curriculum vitae (CV)
    - Protocol
    - Records of receipt and disposition of drugs

  - List of any co-Investigators with their CV
  - Certification that all physicians, dentists, physician's assistants, and/or nurses responsible in the study have appropriate valid licenses for the duration of the investigation, and
  - Emphasis is on toxicity and possible untoward happenings. All unexpected adverse effects are reportable; even if the Investigator considers that the event is not related to the drug. All unexpected, serious adverse effects shall be reported immediately to the IRB in the manner defined by the protocol and this document.
  - IRB letters of approval.
  - Other documents as outlined in the human subject protection program standard operating procedures.

- Investigator-sponsor or Investigator-initiated studies – When an Investigator files an IND or IDE, the Investigator is considered the sponsor and as such is accountable for all of the FDA regulatory responsibilities and reporting obligations of both the PI and the sponsor, as described in the FDA regulations.

An individual or group of individuals or organization is considered a sponsor for an investigation if they hold the IND or IDE.

The research plan asks the Investigator if he/she also acts as the sponsor of the research and, if so, asks him/her to affirm that he/she has reviewed and will comply with the regulatory responsibility of a sponsor.

The sponsor or the Investigator has responsibilities which includes the following:

- Selecting qualified Investigators
- Providing Investigators with the information they need to conduct the investigation properly
- Ensuring proper monitoring of the investigation
- Ensuring that the FDA, any reviewing IRB, and all participating Investigators are promptly informed of significant new information about an investigation.

Additionally, if the IND or IDE product will be manufactured or produced at Pennington Biomedical Research Center, the PI must submit documentation that:

- The product preparation and manufacture meets the standards for current Good Manufacturing Practice (GMP), or any modification to those standards approved by the FDA in issuing the IND or IDE.

- The IND goes into effect 30 days after the FDA receives the IND, unless the sponsor receives earlier notice from the FDA.

The GMP plan has been reviewed by pharmacy, risk management, legal, and compliance issues prior to IRB review. After these offices have reviewed, the GMP plan has been approved by the institutional official. The IRB will periodically conduct random audits of PIs holding an IND or IDE as part of ongoing research compliance efforts.

7.4.2.3 IRB

The IRB will review the research using the same criteria it would use in considering approval of any research involving an FDA-regulated product (FDA 21 CFR 56.111).

All test articles that are dispensed by a pharmacist and administered in a capsule or in a tablet form will be reviewed by the convened board to ensure the safety of the product is reviewed by IRB members with appropriate expertise. Test articles include: drug, biological product for human use, medical device for human use and human food additives.

7.4.3 Expanded Access of Investigational Drugs

FDA regulations allow certain individuals not enrolled in clinical trials to obtain expanded access to investigational drugs, agents, or biologics. Pennington Biomedical Research Center is not a treatment facility, due to these constraints; this institution will not take part in expanded access of investigational drugs.

7.4.4 Emergency Waiver of IND

FDA regulations at 21 CFR 312.34, 312.35, and 312.36 address the need for an Investigational Drug to be used in an emergency situation that does not allow time for submission of an IND. Pennington Biomedical Research Center is not a treatment facility and does not treat patients in an emergency.

7.4.5 Waiver of Informed Consent for Planned Emergency Research

Pennington Biomedical Research Center is a research facility, not a treatment facility; therefore a waiver of informed consent for planned emergency research will not apply to any research completed at this institution.

7.5 Investigational Devices in Research

7.5.1 Policy

Use of an investigational device in a clinical trial to obtain safety and effectiveness data must be conducted according to FDA's IDE regulations found at 21 CFR 812 and other applicable FDA regulations.

The following procedures describe the use of investigational devices in research under the purview of the institution's IRB.

Regulations & Guidelines: FDA 21 CFR 812.00; 21 CFR 812.110; 21 CFR 812.140 (a)

7.5.2 Definitions

***Adverse Device Effect or "ADE")*:** is any adverse event or adverse effect caused by or associated with the use of a device that is unanticipated and has not been included in the protocol or the Investigator's Brochure.

***Device*:** is an instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or other similar or related test article, including a component part, or accessory which is a) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in humans, or b) intended to affect the structure or any function of the body, and which does not achieve any of its primary intended purposes through chemical action within or on the body, and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

***Investigational Device*:** as defined by the FDA, an investigational device is a device that is the object of a clinical study designed to evaluate the safety or effectiveness of the device (21 CFR 812.3 (g)). Investigational devices include transitional devices (21 CFR 812.3 (r)) that are objects of investigations. However, for the purposes of this document, an investigational device may be an approved device that is being studied for an unapproved use or efficacy.

***Investigational Device Exemption ("IDE")*:** is an FDA-approval of the application for an exemption that permits an unmarked device to be shipped for the purpose of doing research on the device (See 21 CFR 812.1 and 812.2 for the scope and applicability).

***Non-Significant Risk Device or NSR Device*:** is an investigational device other than a significant risk device.

***Significant Risk Device "SR Device"*:** is an investigational device that:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a human subject;
- Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a human subject;
- Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presented a potential for serious risk to the health, safety, or welfare or a human subject;
- Otherwise presents a potential for serious risk to the health, safety, or welfare of a human subject.

7.5.3 IDE Requirements

Clinical investigations of devices are subject to the Investigational Device Exemption (IDE) regulations at 21 CFR 812. An approved IDE permits a device that is not approved (via premarket authorization (PMA)) or cleared to market (via 510K) by the FDA to be shipped to conduct clinical investigations of that device. Significant risk devices must have an IDE issued by FDA before they can be shipped. Non-significant risk devices are considered to have an approved IDE when the IRB agrees with the sponsor that the device meets the criteria for a non-significant risk device.

Research with devices falls into three (3) categories:

- Investigations of significant risk devices to determine safety and effectiveness of the device
- Investigations of non-significant risk devices to determine the safety and effectiveness of the device
- Investigations exempted under the regulations

Studies that include medical device use in an incidental way, where the device or the use of the device is not the focus of the research, are generally not considered to be FDA-regulated research or subject to 21 CFR 812, and in some instances are eligible for IRB review according to the expedited procedure (45 CFR 46.110 and 21 CFR 56.110).

The Investigator must indicate on the initial IRB Application whether the research involves investigational drugs or devices. If so, the Investigator must indicate if there is an IND/IDE for the research and provide documented assurance from the sponsor that the manufacture and formulation of investigational or unlicensed test articles conform to federal regulations. Documentation of the IND/IDE could be a:

- Industry sponsored protocol with IND/IDE;

- Letter from the FDA; and
- Letter from industry sponsor

The sponsor is responsible for making the initial risk determination, SR or NSR, and presenting it to the IRB. If the sponsor has determined that a device study is NSR, the IRB will review the sponsor's determination. If the IRB disagrees with the sponsor's NSR assessment and decides the study is SR, the IRB will inform the Investigator and, where appropriate, the sponsor. The IRB will document its SR/NSR determination in the IRB meeting minutes.

For investigational devices, NSR device studies follow abbreviated IDE requirements and do not have to have an IDE application approved by the FDA. If a sponsor has identified a study as non-significant risk, then the Investigator must provide an explanation of the determination. If the FDA has determined that the study is non-significant risk, documentation of that determination must be provided. If the research involves drugs or devices and there is no IND/IDE, the Investigator must provide a rationale why it is not required. The IRB staff will confirm the validity of the IDE number.

Regulations & Guidelines: 21CFR 812; FDA Guidance: IRB Responsibilities for Reviewing the Qualifications of Investigators, Adequacy of Research Sites, and the Determination of Whether an IND/IDE is Needed (2013)

7.5.4 Determination of the Safety and Effectiveness of a Device

The device fulfills the requirements for an abbreviated IDE.

- The device is not a banned device.
- The sponsor labels the device in accordance with 21 CFR 812.5.
- The sponsor obtains IRB approval of the investigation after presenting the reviewing IRB with a brief explanation of why the device is not a significant risk device, and maintains such approval.
- The sponsor ensures that each Investigator participating in an investigation of the device obtains from each subject under the Investigator's care, consent under 21 CFR 50 and documents it, unless documentation is waived.
- The sponsor complies with the requirements of 21 CFR 812.46 with respect to monitoring investigations;
- The sponsor maintains the records required under 21 CFR 812.140(b) (4) and (5) and makes the reports required under 21 CFR 812.150(b) (1) through (3) and (5) through (10);

- The sponsor ensures that participating Investigators maintain the records required by 21 CFR 812.140(a)(3)(i) and make the reports required under 812.150(a) (1), (2), (5), and (7); and
  - The sponsor complies with the prohibitions in 21 CFR 812.7 against promotion and other practices.

7.5.5 Exempted IDE Investigations

For devices, an IDE is not necessary if:

- The research involves a device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time;
- The research involves a device other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of 21 CFR 807 in determining substantial equivalence;
- The research involves a diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10 (c) and if the testing:
  - Is noninvasive;
  - Does not require an invasive sampling procedure that presents significant risk;
  - Does not by design or intention introduce energy into a subject; and
  - Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure;
- The research involves a device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk;
- The research involves a device intended solely for veterinary use;
- The research involves a device shipped solely for research on/or with laboratory animals and labeled in accordance with 21 CFR 812.5 (c); and/or
- The research involves a custom device as defined in 21 CFR 812.3 (b), unless the device is being used to determine safety or effectiveness for commercial distribution.

7.5.6 Responsibilities

7.5.6.1 Principal Investigator

The Investigator is responsible for ensuring that the research is conducted according to all regulatory guidelines, this document, and institutional policies and procedures. The Investigator must obtain approval from the IRB before initiating any research activities or enrolling any subjects in the research.

The Investigator proposing the device research will be required to provide a plan to be evaluated by the IRB that includes storage, security, and dispensing of the device. Elements of a sound control plan include the following:

- ***Storage***: All devices received for a study must be stored in a locked environment under secure control with limited access. The area must be within an area of PI's control. Proper instructions on the use of the device must be provided to the subjects. A log must be kept regarding the receipt, use, and/or dispensing of the device and the disposition of remaining devices at the conclusion of the investigation.
- ***Reporting***: The PI shall report all unanticipated problems involving risk to subjects or others to the IRB according to the procedures outlined in Section 8.
- ***New Device Requirements***: For research involving investigational new drugs:
    - If a device is considered a NSR device by the PI or sponsor, but after review the IRB determines the device to have significant risk, upon receipt of written notice the PI is responsible for notifying the sponsor of the IRBs determination. The PI must provide the IRB with confirmation of this action.
    - If the PI is storing the devices, he/she must maintain a log indicating the identification/serial number of the device, name of subject, date dispensed, by whom it was dispensed, and amount remaining.
    - The PI will maintain the following:
        - Current curriculum vitae CV;
        - Protocol of the study;
        - Records of receipt and disposition of devices;
        - List of any co-Investigators with their CV;
        - Certification that all physicians, dentists, and/or nurses responsible in the study have appropriate valid licenses for the duration of the investigation;

- Case histories with particular documentation on evidence of effects. Emphasis is on safety and possible untoward happenings. All adverse device effects are reportable;
- IRB letters of approval.
- Device training; and
- Other documents as outlined in the Human Subject Protection Program Standard Operating Procedures.

- ***Logs***:
  - The device accountability log must be completed regarding the receipt, use and/or dispensing of the device and the disposition of remaining devices at the conclusion of the investigation; and
  - After use, the Investigator must maintain a log regarding the receipt, use and/or re-dispensing of the device and the disposition of remaining devices at the conclusion of the investigation

- ***Reporting***: The Investigator will submit to the sponsor and to the IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the Investigator first learns of the effect;

- ***Investigator-Sponsor or Investigator-Initiated Studies***: When a PI files an IND or IDE; the PI is considered the sponsor and as such is accountable for all of the FDA regulatory responsibilities and reporting obligations of both the PI and the Sponsor, as described in the FDA regulations.

  An individual or group of individuals or medical center is considered a sponsor for an investigation if they hold the IND or IDE. At Pennington Biomedical these studies are typically called “Investigator initiated studies” when they involve the use an investigational drug or device or use an approved drug or device for investigational purposes.

  The research plan asks the PI if he/she also acts as the sponsor of the research and, if so, asks him/her to *affirm* that he/she has reviewed the **Guidance Document on Requirements of Unsponsored/Investigator-Initiated Research** and will comply with the regulatory responsibilities of a sponsor.

  The sponsors’ or the Investigator as a sponsor responsibilities includes the following:
  - Selecting qualified Investigators;

- Providing Investigators with the information they need to conduct the investigation properly;
- Ensuring proper monitoring of the investigation; and
- Ensuring that the FDA, any reviewing IRBs and all participating Investigators are promptly informed of significant new information about an investigation.

Additionally, if the IND or IDE product will be manufactured or produced at Pennington Biomedical Research Center, the PI must submit documentation that: The product preparation and manufacture meets the standards for current Good Manufacturing Practice (GMP), or any modification to those standards approved by the FDA in issuing the IND or IDE.

The GMP plan has been reviewed by pharmacy, risk management, legal, and compliance issues prior to IRB review. After these offices have reviewed, the GMP plan has been approved by the institutional official. The IRB will periodically conduct random audits of PIs holding an IND or IDE as part of ongoing research compliance efforts.

7.5.6.2 IRB

The IRB will review the research involving investigational devices in accordance with the following requirements and the same criteria it would use in considering approval of any research involving an FDA-regulated product (21 CFR 56.111).

- Control plan;
- Unless the FDA has already made a risk determination for the study, the IRB will review NSR Device studies and determine if the device represents significant or non-significant risk and report the findings to the PI in writing. The IRB will consider the risks and benefits of the medical device compared to the risks and benefits of alternative devices or procedures. NSR Device studies do not require submission of an IDE application but must be conducted in accordance with the abbreviated requirements of IDE regulations. If the study that has been submitted as non-significant risk is considered SR, the IRB may approve the study, but the study cannot begin until an IDE is obtained;
- The IRB will not review protocols involving SR devices under expedited review;
- The IRB determines whether or not the device is a significant risk device.

- The IRB will document in the minutes and provide written documentation to the PI of the rationale for determining whether a device is classified as NSR device/SR device; and
- If the FDA has already made the SR device or NSR device determination for the study, the agency's determination is final and the IRB does not need to make a risk determination.
- If the IRB makes a NSR determination, the IRB will confirm whether the test article met the requirements for an abbreviated IDE

7.5.7 Emergency Use of Unapproved Medical Devices

An unapproved medical device is defined as a device that is used for a purpose or condition for which the device requires, but does not have, an approved application for pre-market approval under section 515 of the FDA Act (21 U.S.C. 360 (e)). Pennington Biomedical Research Center is not a treatment facility; this institution does not conduct the emergency use of unapproved medical devices.

7.5.8 Humanitarian Use Devices (HUD)

Pennington Biomedical Research Center is not a treatment facility; this institution does not conduct research using humanitarian use devices.

8.0 Unanticipated Problems Involving Risks to Subjects or Others

8.1 Policy

Pennington Biomedical Research Center complies with DHHS and FDA regulations which state that institutions must have written policies on reporting unanticipated problems involving risks to subjects or others (as defined below) to the IRB, institutional officials and relevant federal agencies and departments.

The following procedures describe how unanticipated problems involving risk to subjects or others are handled in research under the purview of the Pennington Biomedical Research Center IRB.

8.2 Definitions

Unanticipated Problem Involving Risks to Participants or Others: means any incident, experience, outcome, or new information where all three elements exist:

1. Is unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
2. Is related or possibly related to participation in the research, and
3. Indicates that subjects or others are at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Unexpected Incident: an event or occurrence that is not expected or regarded as unlikely to happen, involves no more than minimal risk to participants or others and does not meet the standard of unanticipated problems involving risks to participants or others.

Unanticipated Adverse Device Effect: Any serious adverse effect on health or safety or any life-threatening problem or death caused by (or associated with) a device, if that effect, problem or death was not previously identified in nature, severity or degree of incidence in the investigational plan or application; any other unanticipated, serious problem associated with a device that relates to the rights, safety or welfare of subjects.

Adverse Event (AE): is any untoward physical or psychological occurrence in a human subject participating in research, including any abnormal sign (e.g., abnormal physical exam or laboratory finding, symptoms or disease associated with the research or the use of a medical investigational test article), symptom, or disease, temporally

associated with the subject's participation in the research. An adverse event does not necessarily have to have a causal relationship with the research, or any risk associated with the research or the research intervention, or the assessment.

Expected Adverse Event: Any event that does not meet the definition of unexpected adverse event.

External (non-local) Adverse Events: Adverse events experienced by subjects enrolled by Investigators at other institutions engaged in a multi-center clinical trial, or a different ongoing clinical trial involving the same intervention.

Internal (local) Adverse Events: Adverse events experienced by subjects enrolled by the Investigator(s) at Pennington or Pennington-related site.

Serious Adverse Event (SAE): An adverse event that is fatal or life-threatening, permanently disabling, requires or prolongs hospitalization or results in significant disability, congenital anomaly or birth defect.

Unexpected Adverse Event: means the incident, experience or outcome is not expected (in terms of nature, severity, or frequency) given the research procedures that are described in the protocol-related documents, such as the IRB approved research protocol and informed consent documents; and the characteristics of the subject population being studied; or are consistent with either:

1. the known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol–related documents, such as the IRB-approved research protocol, any applicable Investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; or
2. the expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.

Others: means individuals other than research participants (e.g., Investigators, research assistants, students, the public, etc.).

Related (or "Possibly Related"): means that there is a reasonable possibility that the event, incident, experience or outcome may have been caused by the procedures involved in the research, underlying disease, disorder, or condition of the subject, or other circumstances unrelated to either the research or any underlying disease, disorder, or condition of the subject. OHRP 7/15/2007 Guidelines

Unrelated: Unassociated or without a timely relationship; evidence exists that an outcome is definitely related to a cause other than the event in question.

8.3 Procedures

All unanticipated problems should be reported regardless of whether they occur during the study, after study completion, or after participant withdrawal or completion. The type of information that must be submitted in a report to the IRB is outlined in the Unanticipated Problem Reporting xForm in IRBManager.

8.3.1 Potential Unanticipated Problems: Adverse Events

In order for an adverse event to meet the definition of an unanticipated problem involving risk to subjects or others, the adverse event must meet the following conditions. It must be *unexpected*, it must be *related or possibly to the research*, and it must suggest that subjects are at greater risk than was previously known or recognized. The Investigator must determine that these conditions are met before reporting the event to the IRB. If the Investigator determines that the incident, experience, or outcome represents an unanticipated problem, a report must be forwarded promptly (see section 8.4) to the IRB. [CFR 46.108(a)(3)(iii)]

Some of the AEs experienced by subjects enrolled in research studies will meet the criteria for unanticipated problems involving risks to subjects or others and so must be reported promptly to the IRB. However, the vast majority of adverse events, both SAEs and non-serious AEs, occurring in the context of research, are expected in light of the known toxicities and side effects of the research procedures or are expected due to the natural history of subjects' underlying diseases and conditions. Thus, most individual AEs do not represent unanticipated problems subject to the reporting requirements outlined in the federal regulations at 45 CFR 46.103(b) (5) and 21 CFR 56.108(b) (1)

8.3.2 Examples of Events that Require Prompt Reporting

1. Internal adverse events that are unexpected, and related or possibly related to the research and that indicate there are new or increased risks to subjects or others;
2. External adverse events that have been determined to be unanticipated problems involving risks to participants or others;
3. Unanticipated adverse device effects that are serious and caused by, or associated with, the device;
4. Changes made to the approved research protocol or plan without IRB approval in order to eliminate apparent immediate harm or hazard to subjects or others;

5. Any accidental or unintentional change to the approved research protocol or plan that placed subjects or others at an increased risk of harm regardless of whether there was actual harm to subjects or others or has the potential to recur;
6. Any event that requires prompt reporting according to the research protocol or investigational plan or the sponsor;
7. Breach of confidentiality or violation of HIPAA (e.g., lost or stolen laptop);
8. Any unanticipated untoward or unfavorable medical occurrence, including abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease that indicated the research places subjects at increased risk of physical or psychological harm than previously known or recognized;
9. Medication, procedural or laboratory error (e.g., errors in drug administration or dosing, surgical or other procedure, or testing of samples or test results) regardless of whether subjects experienced any harm;
10. Interim analysis, safety monitoring report, publication in the literature, or other finding that indicates an unexpected change to the risks or potential benefits of the research;
11. Change in FDA labeling (e.g., black box warning), withdrawal from market, manufacturer alert from the sponsor, or recall of an FDA-approved drug, device, or biologic used in the research;
12. Complaint by/on behalf of a subject that indicates an unanticipated risk or that cannot be resolved by the research staff;
13. Incarceration of a subject during participation in research that is not approved for involvement of prisoners as subjects;
14. Pregnancy of a subject during participation in research that is not approved for involvement of pregnant women as subjects (pregnant women may take part in research only when the IRB has approved the research on Subpart B;
15. Noncompliance with applicable regulations or requirements or determinations of the IRB identified by the research team or others (e.g., FDA Form 483 or Warning Letter) that indicates that the rights, welfare, or safety of subjects have been adversely affected;
16. Suspension or termination of the research, in whole or in part, based on information that indicates that the research places subjects at an increased risk of harm than previously known or recognized (e.g., FDA clinical hold);
17. Suspension or disqualification of an Investigator by FDA, sponsor, or others;
18. Scientific misconduct;
19. Any other problem that indicates that the research places subjects or others at an increased risk of harm or otherwise adversely affect the rights, welfare or safety of subjects or others.

8.3.3 Reporting

All adverse events must be reported to the sponsor. Federal guidelines do not require reporting adverse events to IRBs. They do require that Unanticipated Problems Involving Risks to Subjects or Others [21 CFR 56.108(b)] and Unanticipated Adverse Device Events [21 CFR 812.150(a) (1)] be reported to the IRB CFR 46.108(a)(3)(iii) or (4).

Some adverse events qualify as unanticipated problems that must be reported to the IRB; however, most adverse events do not. When Unanticipated Problems Involving Risks to Subjects or Others or Unanticipated Adverse Device Events are reported to the IRB, and the IRB agrees that they fall into these categories, then the IRB notifies the institution about these events, and the institution notifies FDA and OHRP (as applicable) that these unanticipated problems have occurred when the studies are under their oversight.

Generally, an analysis of adverse event(s) that are an increased risk of harm, related, and unexpected (all three) is the basis for concluding there is an unanticipated problem. These unanticipated problems must be reported to the IRB and usually require some change in the study (revised consent, protocol, or investigational brochure; stopping enrollment; terminating an arm of the study; etc.). These types of analyses are often done by Data Monitoring Committees or similar groups set up by the sponsor.

8.3.4 Local SAEs vs. External (non-local) SAEs / Medwatch Safety Reports

To maximize subject protection, when local adverse events occur that are in the judgment of the Investigator related + unexpected + increased risk of harm, these should be reported along with the Investigator opinion/analysis of whether this rises to the level of an unanticipated problem involving risks to subjects or others, and what if anything should change in the study.

To avoid taking valuable time away from more useful subject protection activities, do not report external adverse events unless there has been an analysis or a judgment made that a particular adverse event or events that are related + unexpected + increased risk of harm have created a signal that has been determined to be an unanticipated problem involving risks to subjects or others. Generally this will mean that something changes in the study (consent form, protocol, Investigator brochure, stop enrollment, one arm will be closed, etc.). This type of analysis is usually done by the sponsor or a Data Monitoring Committee. The local Principal Investigator will rarely have enough data or a denominator to make appropriate conclusions whether there is

a signal that rises to the level of an unanticipated problem involving risks to subjects or others.

8.3.5 Events Not Requiring Prompt Reporting

Potential risks and adverse events that may be reasonably anticipated (i.e., "expected") should be described in the informed consent form.

Potential risks and adverse events that may be reasonably anticipated (i.e., "expected") do not require prompt reporting to the IRB by Investigators and/or research staff. Below are other examples of events that do not require prompt reporting:

- Adverse device effects that are not an increased risk of harm, anticipated, or unrelated
- Adverse events or injuries that are not an increased risk of harm, expected, or unrelated
- Deaths not attributed to the research, e.g., from "natural causes," accidents, or underlying disease and the Investigator has ruled out any connection between the study procedures and the participant's death
- DSMB reports; interim analyses; or other reports, findings, or new information not altering the risk/benefit profile
- Subject complaints that were resolved or complaints not involving risks
- Problems or findings not involving risk (unless the Investigator or research staff member believes the information could affect participants' willingness to continue in the research).

Related internal and external events involving risk but not meeting the prompt reporting requirements should be reported to the IRB in summary form at the time of continuing review. In lieu of a summary of external events, a current DSMB report can be submitted for research subject to oversight by a DSMB (or other monitoring entity).

External events that do not meet the reporting requirements (e.g., not related or not involving risk) and that are not relevant to the protection of participants at Pennington Biomedical Research Center should not be reported. Investigators should retain copies of all individual event reports on file.

8.4 Time Frame for Reporting Unanticipated Problems involving Risks to Subjects or Others

Unanticipated Problems involving risks to subjects or others should be reported within ten (10) working days of the Principal Investigator or research staff becoming aware of

the unanticipated problem. Most often an analysis is required of multiple adverse events to determine whether these met the criteria for an unanticipated problem for the study. The ten (10) working days timer starts when the analysis or determination is made that there is an unanticipated problem.

In device studies, the unanticipated adverse device event (UADE) evaluation by the sponsor must be reported by the sponsor to the IRB within ten (10) working days after the sponsor first receives notice of the UADE. If the UADE occurred at Pennington Biomedical Research Center, the Investigator must report it to the IRB and the sponsor within ten (10) working days.

Events resulting in temporary or permanent interruption of study activities by the Investigator or sponsor to avoid potential harm to subjects should be reported within 48 hours when possible.

8.5 Review Process

8.5.1 Initial Review

Once a report of a potential unanticipated problem is received in the IRB Office the following actions will occur:

- The report will be screened by the HRPP Director or designee in order to determine:
    a. Whether or not the events are possibly unanticipated problems and are related to the research and increase risks to subjects or others. If there are questions regarding the classification of the event, the Chair or designee will be contacted.
    b. Whether or not the currently enrolled or prospective subjects in the trial may be subject to immediate increased harm to their health, safety, or welfare. If a concern arises, the Chair or designee will be promptly contacted and if necessary, the protocol will be suspended or terminated to assure the protection of research participants in accordance with HRPP policy.
- Events that meet the Unanticipated Problems reporting criteria will be sent to the convened board for review. Events that are determined to be Unexpected Incidents involving no more than minimal risk to participants and others will require no further review and will be returned via IRB Manager.
- Reports meeting the criteria will undergo review by the convened IRB.
- The primary reviewer will review the event using the unanticipated problems primary reviewer form. IRB decisions will be communicated to the PI via correspondence in IRBManager.

8.5.2 Convened Review

Reports of events determined during screening or expedited IRB review to represent possible unanticipated problems involving risks to subjects or others will be forwarded to the IRB for convened review. Modifications proposed by the Investigator or IRB reviewer that represent more than minor changes will also be reviewed by the convened IRB. The Chair or other member with relevant expertise will serve as the primary reviewer. Copies of the reports, all other information provided by the Investigator, and current consent documents (or verbal scripts) with any proposed changes will be included in the review materials for each IRB member. Sections from the protocol, previous event reports and other relevant information or reference materials will also be included, as applicable. The complete protocol file will be available to any IRB member upon request prior to or during the convened IRB meeting.

The IRB will determine by convened review whether the event is an unanticipated problem involving risks to subjects or others and if further action is necessary. Action(s) will be based on the nature of the event, degree to which research participants are placed at risk, occurrence of previous problems, etc. The IRB will consider the rights and welfare of participants when suspending, terminating, or modifying research.

If the IRB finds that the event is an unanticipated problem, according to the definition in the policy, the IRB may recommend any of the following actions:

- Requiring modifications to the protocol
- Revising the continuing review timetable
- Modifying the consent process
- Modifying the consent document
- Notifying current participants (e.g. whenever the information may relate to the participant's willingness to continue participation)
- Providing additional information to past participants
- Requiring additional training of the Investigator and/or study staff
- Reconsidering approval
- Requirement that current participants re-consent to participation
- Monitoring of the research
- Monitoring of the consent process
- Referral to other organizational entities
- Suspending the research
- Terminating the research

If, after reviewing a report, the IRB finds that the event is an unanticipated problem or that suspension or termination of approval is warranted, the IRB will, within fifteen (15) working days of the determination:

- Notify the Investigator in writing of its findings.
- Report its findings and recommendations to the institutional official for further reporting to the appropriate federal officials (e.g., OHRP or FDA), for studies under their oversight (see Policy 11 - Reporting to Regulatory Agencies and Institutional Officials).

8.6 Investigator Responsibilities

- The Investigator must consider whether the Unanticipated Problem requires changes to the research protocol or informed consent process/document or other corrective actions are to protect the safety, welfare, or rights of subjects or others. However, any proposed changes must be reviewed and approved by the IRB before being implemented, except when necessary to eliminate apparent immediate hazard to subjects.
- Investigators are responsible for reporting all adverse events and unanticipated problems to the sponsor.

9.0 Protocol Deviations

Investigators are responsible for conducting human subjects research in compliance with all applicable federal and state regulations and the institution's HRPP policies and procedures. Federal Regulations require the IRB to review any proposed changes in approved research activities prior to their initiation (except when the change is necessary to eliminate apparent immediate hazards to the subject) [45 CFR 46.103(b) (4) (iii) and 21 CFR 56.108(a) (4)].

9.1 Planned Changes to Research Protocol

With regard to planned changes to a research protocol, the most common occurs through the submission of a modification. Examples include an increase in subject number, changes in investigators or key personnel, a change to the funding source, changes in procedures and revised consent documents. These all involve planned changes through an amended protocol and are not protocol deviations themselves (although they may result from a protocol deviation).

Another type of planned change to a protocol is a change made to eliminate apparent immediate harm to a subject. This type of change can be initiated without prior IRB approval, provided that subsequent IRB approval is obtained.

9.2 Unplanned Changes to Research Protocol

The next category involves unplanned changes to a research protocol not otherwise approved by the IRB. Such unplanned changes are protocol deviations.

9.3 Protocol Deviations

A protocol deviation is any change or alteration from the procedures stated in the study protocol, consent document, recruitment process, study materials (e.g. questionnaires) approved by the IRB and/or HRPP or Institutional policies. Protocol deviation is a general term and includes changes made to avoid immediate harm to subjects and protocol violations. [45 CFR 46.103 (b) (4) (iii), 21 CFR 56.108 (a) (4)]. Protocol deviations can be either major or minor. Protocol deviations can be considered either non-serious or serious non-compliance. See Policy 10 – Non-Compliance.

Repeated failure by an investigator to not report protocol deviations may be viewed as non-compliance with the federal regulations, the guidelines that govern ethical conduct of research and Pennington Biomedical Research Center IRB.

9.4 Protocol Violation

The Common Rule and the FDA regulations do not define this term. For the purpose of this policy a violation will be referred to as a deviation.

9.5 Major Protocol Deviation

A major protocol deviation is a deviation that has the potential to impact subject safety or risk, to affect the integrity of the data or to affect the subject's willingness to participate in the study. Major protocol deviations can vary in the degree of seriousness according to how the changes impact subject safety or risk, the effect on the integrity of the data, the effect on the subject's willingness to participate in the study, the degree of non-compliance with federal regulations, state laws, the Pennington Biomedical Research Center's IRB and the degree of foreknowledge of the event.

9.5.1 Reporting Time Frame of Major Protocol Deviation

All major protocol deviations must be reported by the investigator to the IRB within ten (10) working days of learning of the deviation. If it is necessary to make a permanent change to the study procedures in order to avoid harm to other subjects, then a protocol modification should be submitted as soon as possible by the investigator. If appropriate to maintain safety of the subjects, new subject enrollment should be temporarily stopped by the investigator until the modification is approved.

No matter who discovers a major protocol deviation (e.g., sponsor or their agent during a monitoring visit), the investigator is responsible for reporting it to the IRB.

9.6 Minor Protocol Deviation

A minor protocol deviation is one that does not have the potential to impact subject safety or risk, compromise the integrity of the study data, or affect the subject's willingness to participate in the study.

9.6.1 Reporting Time Frame for Minor Protocol Deviations

All minor deviations should be reported by the investigator in a protocol-specific minor deviation log and submitted to the IRB at continuing review or IRB closure.

9.7 Investigator Responsibility

It is the responsibility of the Principal Investigator (PI) to determine whether a deviation from the IRB-approved protocol is major or minor and to ensure proper reporting to the IRB. When making the determination of whether the deviation is major or minor, the

Principal Investigator should consider whether the deviation negatively affected any of the following:

- The rights or welfare of the subject
- Risk benefit assessment
- The integrity of the data (the ability to draw conclusions from the study data)

The Principal Investigator is responsible for reviewing the Minor Deviation Log periodically to monitor compliance with the approved research. Frequent minor deviations of a similar nature should be reported to the IRB as a major deviation.

All protocol deviations should be reported to the research sponsor or funding agency in a timely fashion and according to that company's or agency's policy.

9.8 IRB Review Process

9.8.1 Protocol Deviations

The IRB Chair or designee will review the major deviation and determine whether immediate action is required before review at the convened IRB. All major protocol deviations must be summarized in the appropriate section of the continuing review form. Minor deviations must be included in a log at the time of continuing review or IRB closure.

Each protocol deviation reported to the IRB should discuss what measures have been put in place to prevent future recurrences of the same event. The investigator should also evaluate protocol deviations for any trends or patterns that would require additional corrective actions or submission of a protocol modification to prevent future deviations. Repeated deviations of a similar nature may be a clear indication that a permanent change (i.e. a modification) to the study procedures is necessary.

9.8.2 Review of Deviations

For studies reviewed under expedited review procedures, all major deviations will be reviewed by the convened IRB.

For protocol deviations that require fully convened IRB review, the assigned IRB reviewer will document the determinations and outcomes. The determinations and outcomes will be reported in the IRB minutes. The investigator will receive a notification of determination from the IRB. The potential determinations are as follows:

- No further action is required.
- Request additional information.
- The deviation appears to be serious or continuing non-compliance may be involved.

- The deviation represents an unanticipated problem involving risks to participants or others (must be handled according to Policy 8 - Unanticipated Problems Involving Risks to Subjects or Others)
- Suspend IRB approval of the research
- Other (e.g., modify the protocol, observe informed consent process, alter continuing review timeline, require additional training of investigators and/or study staff). The reviewer must specify the action and document the determination.

For Federal reporting purposes, the IRB will need to determine whether the protocol deviation constitutes an instance of serious or continuing non-compliance. If the protocol deviation is an event involving a change in the protocol to eliminate immediate hazard or harm to subjects, the IRB should ensure that the event was reported in the required 10-day period. Also, the IRB should make certain that the investigator implemented appropriate measures to alleviate or eliminate the harm to current and future subjects in the research.

Pennington Biomedical Research Center investigators are not required to report protocol deviations to the IRB that occur at other research sites in multi-center research trials. The investigator may have other reporting requirements such as reporting to Institutional Biosafety Committee, and/or other appropriate institutional entities that are not covered in this policy.

9.9 Examples of Deviations

This list of examples is intended as a guide and is not exhaustive.

Major Deviations Examples	**Minor Deviations Examples**

• Deviation from inclusion/exclusion criteria.
• Changes necessary to eliminate apparent immediate hazards to the subject
• Breach of human participants protection regulations
• Failure to obtain informed consent prior to initiation of study–related procedures
• Inadequate or improper informed consent procedures (including no documentation of informed consent process)
• Performing tests or procedures beyond those anticipated in the protocol unless performed to rule out a medical condition
• Falsifying research or medical records
• Working under an expired professional license or certification
• Inappropriate destruction of study records
• Failure to report a serious adverse event to the IRB and/or sponsor
• Enrollment of a participant after IRB-approval of study has expired
• Failure to perform a required lab test that, in the opinion of the PI, may affect subject safety or data integrity
• Drug/study medication dispensing or dosing error
• Study visit conducted outside of required timeframe that, in the opinion of the PI, may affect subject safety
• Failure to follow safety monitoring plan
• Participant discontinued study meds
• Participant misses visits involving study drug
• Participant did not disclose metal and had MRI
	• Missing original signed and dated consent form (only a photocopy available)
	• Outdated/expired consent form, as long as there has been no impact on participant safety
	• Missing pages from executed consent form
	• Failure to follow the approved study procedure, that in the opinion of the Principal Investigator, does not affect the participant safety or data integrity:
	  ○ Study procedures conducted out of sequence
	  ○ Omitting an IRB approved research activity on a protocol (e.g. mailing out or collecting QOL surveys, evaluating or documenting performance status), unless the omission could affect safety
	  ○ Failure to perform a required lab test that does not affect participant safety.
	• Inappropriate documentation of informed consent, including
	  ○ copy not given to the person signing the form
	  ○ someone other than the subject dated the consent form
	• Over-enrollment
	• Participant misses visits due to following:
	  ○ Inclement weather
	  ○ Employment change
	  ○ Rescheduling for other reasons that do not involve safety and do not compromise the integrity of the data
	  ○ Procedures not completed at participant's request
	• Testing outside of protocol timeframe due to the following:

	○ Inclement weather ○ Time and burden ○ Rescheduling for other reasons that do not involve safety and do not compromise the integrity of the data ○ Failure of subject to return study medication

10.0 Complaints and Non-compliance

10.1 Policy

As part of its commitment to protecting the rights and welfare of human subjects in research, Pennington Biomedical Research Center reviews all complaints and allegations of non-compliance and takes any necessary action to ensure the ethical conduct of research.

All investigators and other study personnel involved in human subject's research are required to comply with all laws and regulations governing their research activities, as well as with requirements and determinations of the IRB. Research participants or others are encouraged by the institution to report to the IRB Office any complaints or allegations of noncompliance.

The following procedures describe how complaints, concerns and allegations of non-compliance are handled by the IRB. In cases where serious non-compliance or continuing non-compliance has occurred, the IRB may exercise its authority to monitor, suspend, or terminate the research.

Regulations & Guidance: DHHS 45 CFR §46.103(b)(5)(i); 45 CFR §46.116(b)(5); FDA 21 CFR §50.25(b)(5); 21 CFR §56.108(b)(2); OHRP Guidance on Reporting Incidents to OHRP.

10.2 Definitions

Allegation of non-compliance: is defined as an unproven assertion of non-compliance.

Non-compliance: is the failure to follow federal, state, or local regulations governing human subject research, institutional policies related to human subject research, or the requirements or determinations of the IRB.

Continuing non-compliance: A pattern of non-compliance which

- continues after initial discovery or IRB approval of corrective action plan or
- is initially discovered to have already occurred more than once and suggests that non-compliance will continue if there is no intervention, or
- increases the risk of serious non-compliance, or
- if continued, could potentially significantly increase risks to, or jeopardize the safety, welfare, and/or rights of subjects or others, or

- if continued, could decrease potential benefits (the scientific integrity of the research).

Serious non-compliance: Non-compliance that potentially creates an increase in risks to subjects, adversely affects the rights, welfare and safety of the research subjects or adversely affects the scientific integrity of the study. Willful violation of policies and/or federal regulations may also constitute serious non-compliance.

Examples of non-compliance

- Failure to follow any of the regulations and policies described in the HRPP policy
- Failure to follow the determinations of the IRB
- Research being conducted without prior IRB approval

Regulations and Guidance: OHRP Guidance on Reporting Incidents to OHRP.

10.3 Initial Assessment

The HRPP Director will promptly handle (or delegate staff to handle) and, if necessary, investigate all complaints, concerns, reports and allegations of noncompliance received by the IRB. This includes complaints, concerns and appeals from investigators, research participants and others.

All complaints, written or verbal (including telephone complaints), and regardless of point of origin and funding source are recorded by IRB staff and forwarded to the IRB chairperson/designee.

Initial assessment of the validity of a report will be made by the HRPP Director in consultation with the IRB chairperson/designee, Director of Legal and Regulatory Compliance or appropriate official within institution as needed. If the report has no basis in fact or cannot be adequately investigated given the information received, the IRB staff will acknowledge receipt in IRB Manager and no further action will be taken.

The initial assessment may include, but is not limited to, a review of the approved consent document, protocol, speaking with study staff, or a review of financial records associated the study fund.

The initial assessment will include a determination by the IRB chairperson/designee of whether the complaint warrants immediate suspension of the research project. If a suspension is warranted, the procedures in section 3.11 - Study Suspension, Termination and Investigator Hold will be followed.

If the report meets the definition of Non-Compliance, it will be considered an allegation of non-compliance according to section 10.4 – Non-Compliance.

If the report meets the definition of an unanticipated problem, it will be handled according to HRPP policy 8- Unanticipated Problems Involving Risks to Subjects or Others.

If the report meets the definition of a deviation, it will be handled according to HRPP policy 9 – Protocol Deviations.

If the report meets the definition of scientific misconduct, it will be handled according to PBRC policy 285.00 – Misconduct in Research.

Generally within 10 working days of the initial assessment, the IRB chairperson/designee shall generate a letter to acknowledge that the report has been received and is being investigated to the party that reported the incident, if a follow-up contact name is provided.

10.4 Non-Compliance

Investigators and their study staff are required to report instances of possible non-compliance. The investigator is responsible for reporting any possible non-compliance by study personnel to the IRB. Principal investigators are required to report results of audits or inspections conducted by sponsors, other external entities such as the Food and Drug Administration (FDA), or internal oversight committees, which indicate noncompliance. Common reports to the IRB that are serious or continuing are typically protocol deviations/violations. However, any individual or employee may report observed or apparent instances of non-compliance to the IRB. In such cases, the reporting party is responsible for making these reports in good faith, maintaining confidentiality and cooperating with any IRB and/or institutional review of these reports. Pennington Biomedical will take reasonable steps to protect persons who file reports in good faith from retaliatory actions based on such filing, in accordance with federal, state and local law.

If an individual, whether investigator, study staff or other, is uncertain whether there is cause to report non-compliance, he or she may contact the IRB chairperson/designee or IRB Staff directly to discuss the situation informally.

Reports of non-compliance must be submitted to the IRB office within 10 working days of discovery of this non-compliance. The report must include a complete description of the non-compliance and the personnel involved.

Regulations & Guidance: FDA 21 CFR §56.108(b).

10.4.1 Review of Allegations of Non-Compliance

Reports of non-compliance can include but are not limited to, protocol deviations, unanticipated events involving risks to subjects or others, complaints from participants or others regarding treatment by research staff, reimbursement issues, issues of data integrity, or any other compliance concerns. When a report of non-compliance is made by someone other than the principal investigator, effort will be taken to maintain confidentiality. The name of the reporter will not be disclosed to the individuals involved in the complaint, unless disclosure is required to reconcile the situation.

IRB staff may receive an allegation of non-compliance by any means including, but not limited to:

- voluntary notification by the principal investigator or research staff, through IRB Manager or direct communication with the IRB staff
- information given by other staff of the institution,
- information given by other members of the research staff,
- monitoring reports provided by the study sponsor,
- reports of non-compliance by research subjects via the telephone number listed on all approved informed consent documents
- anonymous reports

When a recommendation of non-compliance is made because the incident was within the limits of an approved protocol for the research involved, the determination is reported by the IRB in writing to the investigator following the review and, if applicable, the reporting party.

If in the judgment of the reviewer, any allegation or findings of non-compliance is considered true, the non-compliance will be processed according to section 10.4.2 – Review of Findings of Non-Compliance.

If in the judgment of the IRB, any allegation or findings of non-compliance warrants suspension of the research before completion of any review or investigation to ensure protection of the rights and welfare of participants, the IRB chairperson/designee may suspend the research as described in section 3.11- Study Suspension, Termination and Investigator Hold with subsequent review by the IRB.

The HRPP Director with the assistance of the IRB chairperson/designee may determine that additional expertise or assistance is required to make these determinations and may form a sub-committee to assist with the review and fact gathering process. See 10.4.3 – Subcommittee Procedures.

10.4.2 Review of Findings of Non-Compliance

10.4.2.1 Non-compliance is Not Serious or Continuing

When the IRB determines that non-compliance occurred, but the non-compliance does not meet definition of serious non-compliance or continuing non-compliance, the determination is reported in writing to the investigator and if applicable the reporting party. The investigator will develop a corrective action plan to prevent future non-compliance, which will be reviewed by the IRB to confirm it's adequate. The report of non-compliance and corrective action is reported to the IRB and reflected in the IRB minutes. If however, the investigator refuses to cooperate with the corrective action plan, the matter is referred to a convened meeting of the IRB with notification to the Institutional Official.

10.4.2.2 Serious Non-Compliance or Continuing Non-Compliance

When the HRPP Director or the IRB chairperson/designee determines that non-compliance has occurred and that the non-compliance meets the definition of serious non-compliance or continuing non-compliance, the report of non-compliance is referred for review by the IRB at the next convened available meeting. However, the HRPP Director with the support of the IRB chairperson/designee may use discretion and call an emergency IRB meeting should the circumstances warrant such an urgent meeting or determine the non-compliance needs further review by the sub-committee.

Examples of serious non-compliance may include the following, but are not limited to: falsifying IRB documents; conducting human subject's research without IRB approval; deviating from the IRB approved protocol or consent process; modifying the protocol or consent process without prior IRB approval.

All findings of serious or continuing non-compliance referred to the IRB will be reviewed at a convened meeting. All IRB members will receive:

- All documents relevant to the allegation,
- The last approved IRB protocol; and
- The last approved consent document.

At this stage, the IRB may:

- Find that there is no issue of Non-Compliance
- Find that there is non-compliance that is neither serious non-compliance nor continuing non-compliance and an adequate corrective action plan is in place

- Find that there is serious or continuing non-compliance and approve any recommended determinations proposed by the IRB chairperson/designee and/or sub-committee
- Request additional information.

10.4.3 Sub-Committee Procedures

The HRPP Director or the IRB chairperson/designee may appoint a subcommittee consisting of IRB members, and non-members if appropriate, to ensure fairness and expertise. The subcommittee is given a charge by the IRB, which can include any or all of the following:

1. Review of protocol(s) in question;
2. Review of sponsor audit report of the investigator, if appropriate;
3. Review of any relevant documentation, including consent documents, case report forms, subject's investigational and/or medical files etc., as they relate to the investigator's execution of her/his study involving human subjects;
4. Interview of appropriate personnel if necessary;
5. Preparation of either a written or oral report of the findings, which is presented to the convened IRB at its next meeting;
6. Recommend actions if appropriate.

The sub-committee will substantiate the findings of serious or non-serious non-compliance in writing to the convened IRB for review. The HRPP Director (or designee) is responsible for assuring that minutes of the meeting are generated and kept to help support any determinations or findings made by the sub-committee.

The report will include any recommended actions. These recommended actions are described in 10.4.4 – Final Review.

10.4.4 Referral to Others

At any point during the initial fact gathering process or later, when the HRPP Director with consultation from IRB chairperson/designee determines that the facts raise issues apart from or in addition to noncompliance with applicable federal, state, and local laws and regulations or the requirements or determinations of the IRB, the HRPP Director shall notify or refer the matter or relevant aspects of the matter to others within the institution for review or other remedial or correction action.

10.4.5 Temporary Suspension (Hold) or Termination of Research

10.4.5.1 Voluntary Hold Placed on Research by the Investigator

The Principal Investigator (PI) may voluntarily place the research on hold in whole or in part while the investigation into reports of noncompliance is being conducted. Such temporary holds are not subject to the reporting requirements in 45 CFR 46.103(b)(5) and 21 CFR 56.108(b)(2).

10.4.5.2 Temporary Suspension or Termination of Research by the IRB

At any point during the initial fact gathering process or later, the IRB chairperson or designee may temporarily suspend in whole or in part or terminate the research.

Such suspensions or terminations will be reported in accordance with Pennington Biomedical Research Center policy (see section 3.11.1 – Suspension or Termination)

10.4.6 Final Review

The convened IRB and/or the results from the subcommittee will be reviewed at a convened IRB meeting. When there is a finding of non-compliance, the IRB's possible actions could include, but are not limited to:

1. Request a correction action plan from the investigator
2. Verification that participant selection is appropriate and observation of the actual informed consent
3. An increase in data and safety monitoring of the research activity
4. Request a directed audit of targeted areas of concern
5. Request a status report after each participant receives intervention
6. Modify the continuing review cycle
7. Request additional investigator and staff education
8. Notify current subjects, if the information about the non-compliance might affect their willingness to continue participation
9. Require modification of the protocol
10. Require modification of the information disclosed during the consent process
11. Require current participants to re-consent to participation
12. Require additional information be given to past participants
13. Suspend the study (see below)
14. Terminate the study (see below)
15. Defer to the Research Integrity Officer and the Institutional Official

In cases where the IRB determines that the event of non-compliance also meets the definition of unanticipated problem, the policy and procedure for review of such events will also be followed.

The investigator is informed of the IRB determination and the basis for the determination in writing and is given a chance to respond. If the IRB determines that the non-compliance was serious or continuing, the results of the final review will be reported as described HRPP policy 11 - Reporting to Regulatory Agencies and Institutional Officials.

10.4.7 Reinstatement of a Suspended Study

The corrective action(s) and stipulations necessary for the IRB to consider reinstatement of the research must be decided by the convened IRB. The approval will be described in written correspondence to the Principal Investigator.

10.5 Audits

Audit reports will be generated for each audit investigation and will be distributed to the principal investigator. For routine audits, the HRPP Director or designee will conduct an initial review of the audit report. If the audit report contains no findings related to serious or continuing non-compliance, the audit report can be accepted as written on behalf of the IRB. A copy of the audit report may be placed on the next agenda for IRB members to review for informational purposes.

The HRPP Director may work with the principal investigator, if requested, to implement any recommendations that were included in the audit report. Failure by the principal investigator to communicate to the IRB Office regarding implementation of recommendations may lead to a “for cause” audit or could be reported to the IRB as continuing non-compliance.

All audit reports that result from “for cause” audits, regardless of the findings, and any audit reports that either the HRPP Director or the IRB chairperson/designee (or both) determine to include findings of serious or continuing non-compliance will be placed on the next IRB agenda for review at a convened meeting of the IRB. Audit reports will be available for review by all IRB members.

Following the IRB’s review of the audit report and any additional determinations that they have made, the principal investigator will be notified (via IRB Manager) of the outcome of the review. If the IRB offers a plan of correction, the specific changes to be implemented will be communicated, as well as a time frame for implementing the changes. If the IRB has determined that the project is to be suspended or terminated, this information will be communicated to the principal investigator as well, and handled

according to the IRB review process (Policy 3) and the reporting to authorities (Policy 11).

11.0 Reporting to Regulatory Agencies and Institutional Officials

11.1 Policy

Federal regulations require prompt reporting to appropriate institutional officials and the department or agency head of any unanticipated problem involving risks to subjects or others, any serious non-compliance or continuing non-compliance with the HRPP or institutional policies or the requirements or determinations of the IRB; and any suspension or termination of IRB approval.

The Federalwide Assurance (FWA) of the institution is designated to apply to federally supported or conducted human-subjects research. In general, the same criteria and process for the conduct and oversight of human-subjects research, for determinations about reportable events, and for actions taken in response to such events will apply to all human-subjects research in which institution is engaged, regardless of funding source.

In addition to the reporting requirements to institutional officials and regulatory agencies, the IRB is responsible for reporting any major event to the Association for the Accreditation of Human Research Protection Programs (AAHRPP) to comply with AAHRPP's reporting requirements for accredited organizations.

The IRB will comply with this requirement and the following procedures describe how these reports are handled.

Regulation [CFR 46.108(a)(3)(iii)]

11.2 Procedures

- IRB staff will initiate these procedures as soon as the IRB takes any of the following actions:
    - Determines that an event may be considered an unanticipated problem
    - Determines that non-compliance was serious or continuing
    - Suspends or terminates approval of research
- The IRB staff is responsible for preparing reports or letters which includes the following information:
    - The nature of the event (unanticipated problem involving risks to subjects or others, serious or continuing non-compliance, suspension or termination of approval of research)
    - Name of the institution conducting the research

- Title of the research project and/or grant proposal in which the problem occurred
- Name of the principal investigator on the protocol
- Number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement)
- A detailed description of the problem including the findings of the organization and the reasons for the IRB's decision
- Actions the institution is taking or plans to take to address the problem (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.)
- Plans, if any, to send a follow-up or final report:
  - With a specific date defined
  - When an investigation has been completed or a corrective action plan has been implemented

- The IRB Chair and the institutional official will review the letter and modify the letter/report as needed.
- The institutional official is the signatory for all correspondence from the facility to the regulatory agencies.
- The IRB staff sends a copy of the report to:
  - The IRB by including the letter in the next agenda packet as an informational item
  - The Institutional Official
  - Report to the Research Integrity Officer, if a finding of non-compliance was serious or continuing
  - The following federal agencies:
    - OHRP, if the study is subject to DHHS regulations or subject to a DHHS Federal-wide Assurance
    - FDA, if the study is subject to FDA regulations.
    - DOD, if the study is subject to Department of Defense regulations
    - If the study is conducted or funded by any federal agency other than DHHS that is subject to *The Common Rule*, the report is sent to OHRP or the head of the agency as required by the agency

      Note: Reporting to a regulatory agency is not required if the event occurred at a site that was not subject to the direct oversight of the organization, and the agency has been notified of the event by the investigator, sponsor, another organization, or other mechanisms.

- Principal investigator
- Sponsor, if the study is sponsored
- Contract research organization (CRO), if the study is overseen by a contract research organization
- Other sites involved in the research when appropriate
- Others as deemed appropriate by the institutional official

The IRB Chair ensures that all steps of this policy are completed within 15 working days of the initiating action. For more serious actions, the IRB Chair will expedite reporting.

12.0 Investigator Responsibilities

12.1 Policy

Investigators are ultimately responsible for the conduct of research. Research must be conducted according to the signed Investigator statement, the investigational plan and applicable regulations for protecting the rights, safety, and welfare of subjects under the Investigator's care. Investigators may delegate research responsibility. However, Investigators must maintain oversight and retain ultimate responsibility for the conduct of those to whom they delegate responsibility.

The following procedures describe the Investigator responsibilities in the conduct of research involving human participants.

12.2 Definitions

Principal Investigator ("PI", "Co-I" or "Investigator"): is an individual who conducts research or under whose immediate direction research is conducted; or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team. NIH PHS 398

Investigator means an individual who actually conducts a clinical investigation, i.e., under whose immediate direction the test article is administered or dispensed to, or used involving, a subject, or, in the event of an investigation conducted by a team of individuals, is the responsible leader of that team. FDA 21 CFR 50.3.25(d)

Researcher: is the PI and/or Investigator.

Research Team: is defined as the Investigator and other individuals, also known as key personnel, who contribute to the scientific development or execution of a project in a substantive, measurable way, whether or not they receive salaries or compensation under the protocol.

12.3 Investigators

12.3.1 Principal Investigators

For the purposes of this institution, Principal Investigators must be on staff (paid employee), adjunct faculty, or a member of the faculty of one of the institutions affiliated with the Pennington Biomedical Research Center. Professionals in training (graduate students, post-doctoral researchers, interns, and residents) are permitted to be Principal Investigators as long as permitted by their home institution policies. Fellows may be Principal Investigators if they have attending privileges at the

Institution. In order to serve as a Principal Investigator, any person who is not a member of the regular faculty must have at least one regular faculty member as a Co-Investigator on the project.

12.3.2 Change in Principal Investigator

If there is a change in the PI, the outgoing Investigator must submit a modification to previously approved research to notify the IRB that he or she has relinquished the responsibilities of the Investigator to the person named, or will do so on a specific date. The newly named Investigator notifies the IRB that he or she has read the protocol and agrees to accept the responsibilities of the Investigator.

12.3.3 Student Investigators

Students may not serve as Investigators. They must have a Pennington Biomedical Research Center employee who fulfills the Investigator eligibility criteria and who will serve as Investigator on the study. (See Policy 302 Human Research Protections Program Policy section 1.3.2 for the definition of Principal Investigator)

12.4 Responsibilities

In order to satisfy the requirements of this policy, Investigators who conduct research involving human subjects must:

1. Develop and conduct research that is in accordance with the ethical principles in the Belmont Report
2. Develop a research plan that is scientifically sound and minimizes risk to the subjects
3. Have sufficient resources necessary to protect human subjects, including:
    - Access to a population that would allow recruitment of the required number of subjects
    - Sufficient time to conduct and complete the research
    - Adequate number of qualified staff
    - Adequate facilities
    - A process to ensure that all persons assisting with the research are adequately informed about the protocol and their research-related duties and functions
    - Availability of medical or psychological resources that subjects might require as a consequence of the research
4. Assure that all procedures in a study are performed with the appropriate level of supervision and only by individuals who are licensed or otherwise qualified to

perform such under the laws of Louisiana and the policies of Pennington Biomedical Research Center

5. Maintain a list of appropriately qualified persons to whom they have delegated significant clinical trial-related duties.
6. Assure that all key personnel are educated in the regulatory requirements regarding the conduct of research and the ethical principles upon which they are based
7. Protect the rights and welfare of prospective subjects
8. Ensure that risks to subjects are minimized:
    - By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and
    - Whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes
9. Recruit subjects in a fair and equitable manner
10. Obtain and document informed consent as required by the IRB and ensuring that no human subject is involved in the research prior to obtaining their consent
11. Have plans to monitor the data collected for the safety of research subjects
12. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons, include additional safeguards in the study to protect the rights and welfare of these subjects
13. Have a procedure to receive complaints or requests for additional information from subjects and respond appropriately
14. Ensure that pertinent laws, regulations, and Institutional procedures and guidelines are observed by participating Investigators and research staff
15. Ensure that all research that qualifies as human subjects receives IRB review and approval in writing before commencement of the research
16. Comply with all IRB decisions, conditions, and requirements
17. Ensure that protocols receive timely continuing IRB review and approval
18. Report unanticipated problems involving risk to subjects or other or any other reportable events to the IRB
19. Obtain IRB review and approval in writing before changes are made to approved protocols or consent forms

20. Seek IRB assistance when in doubt about whether proposed research requires IRB review.
21. Follow the clinical trial's randomization procedures, if any, and ensures that the code is broken only in accordance with the protocol. If the clinical trial is blinded, the researcher promptly documents and explains to the Sponsor any premature unblinding.
22. A qualified physician (or dentist, when appropriate), who is a researcher or a co-researcher for the clinical trial, is responsible for all clinical trial-related medical (or dental) decisions (not applicable to independent IRB's).
23. Inform participants when medical care is needed for other illnesses of which the researchers become aware.
24. If medically necessary and the participant agrees, the researcher will inform the participant's primary physician or specialist about their participation in the clinical trial.
25. Although a participant is not obliged to give his or her reasons for withdrawing prematurely from a clinical trial, the researcher makes a reasonable effort to ascertain the reason, while fully respecting the participant's rights.
26. Provide evidence of his or her qualifications through up-to-date curriculum vitae or other relevant documentation requested by the sponsor, the IRB, or the regulatory authority.
27. Familiar with the appropriate use of the investigational product, as described in the protocol, in the current Investigator Brochure, in the product information, and in other information sources provided by the sponsor.
28. During and following a participant's participation in a clinical trial, the researcher ensures that adequate medical care is provided to a participant for any adverse events, including clinically significant laboratory values, related to the clinical trial (not applicable to independent IRBs).
29. Ensure the accuracy, completeness, legibility, and timeliness of the data reported to the sponsor.
30. Permit monitoring and auditing by the sponsor and inspection by the appropriate regulatory authority.
31. Report all serious adverse events (SAEs) to the sponsor except for those SAEs that the protocol or other document (e.g., Investigator's Brochure) identifies as not needing immediate reporting. The researcher follows regulatory requirements related to the reporting of unexpected serious adverse drug reactions to the regulatory authority and the IRB.

32. Report adverse events or laboratory abnormalities identified in the protocol as critical to safety evaluations to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol.
33. For reported deaths, the researcher supplies the sponsor and the IRB with any additional requested information (e.g., autopsy reports and terminal medical reports).
34. Provide written reports to the sponsor, the IRB, and, where applicable, the organization on any changes significantly affecting the conduct of the clinical trial or increasing the risk to participants.
35. If the researcher terminates or suspends a clinical trial without prior agreement of the sponsor, the researcher informs the organization, sponsor, and the IRB.
36. If the IRB terminates or suspends approval of the clinical trial, the researcher promptly notifies the sponsor.
37. Upon completion of the clinical trial, the researcher informs the organization; the IRB with a summary of the trial's outcome; and the regulatory authority with any reports required.
38. The investigator/institution should conduct the trial in compliance with the protocol agreed to by the sponsor and, if required, by the regulatory authority (ies) and which was given approval/favorable opinion by the IRB.
39. The investigator should be aware of, and should comply with, GCP and the applicable regulatory requirements.

    Regulations & Guidelines: FDA 21 CFR 312.53(c) (1); 21 CFR 312.60; 21 CFR 312.61; 21 CFR 312.62; 21 CFR 812.43(c) (4); 21 CFR 812.100; 21 CFR 812.140, GCP

12.5 Training / Ongoing Education of Investigators and Research Team

As stated above, one component of a comprehensive HRPP is an education program for all individuals involved with research subjects. Pennington Biomedical Research Center is committed to providing training and an on-going educational process for Investigators and members of their research team related to ethical concerns, Federal and State regulatory requirements and Pennington Biomedical Research Center policies for the protection of human subjects. Research teams consist of anyone working directly with human subjects or with identifiable data or biological specimens for research under the purview of the Institution. This includes Investigators, research nurses, coordinators, students, faculty and technicians working with identifiable data. It is the responsibility of the Investigator to ensure that the research team is compliant

with all initial and ongoing education as required by Pennington Biomedical Research Center polices and regulatory requirements.

This requirement is mandatory regardless of funding sources. The requirements also apply to research that is considered exempt from IRB review.

Regulations & Guidelines: DHHS 45 CFR 46.102(d): 45 CFR 46.102(f); FDA 21 CFR50.3(c); 21 CFR 50.3(g); 21 CFR 50.3(j); 21 CFR 56.102(c); 21 CFR 56.102(l)

12.5.1 Initial Education

All Investigators, research team and key personnel are required to complete CITI training every three years as per Pennington Biomedical Research Center Policy 106.00. This policy is managed and tracked by the Director of Legal and Regulatory Compliance.

New research protocols and applications for continuing review will not be accepted or receive final approval until all sub-Investigators and members of the research team have completed the education requirements.

12.5.2 Waiver of Initial Education

If Investigators or members of their research team have successfully completed human subject research training equivalent to that required by the Institution within the last year, they may request a waiver of the requirement for initial education. Please contact the Director of Legal and Regulatory Compliance for more information about obtaining a waiver of education.

12.5.3 Continuing Education and Recertification

All Investigators and members of their research teams must meet Institutional continuing education requirements every three years after certification of initial education for as long as they are involved in human subject research. There is no exception to this requirement. Acceptable refresher modules at the CITI web-based training site must be completed. See PBRC Policy 106.00 for more information.

Investigators must submit evidence of continuing education prior to the expiration of their training certification. New research protocols and applications for continuing review will not be accepted from Investigators who have not submitted satisfactory evidence of continuing education.

Investigators who are also IRB Chair, IRB members, or IRB staff will satisfy the training requirements for IRB members and staff described in this policy under PBRC Policy 106.00.

12.5.4 Investigator Notification of Responsibilities

All policies and procedures including Investigator responsibilities, training and education, guidances and contact information for the HRPP are listed on the HRPP website found at www.pbrc.edu/HRPP. Investigators are notified via email of changes to the HRPP and are directed to the HRPP website which details the changes.

12.5.5 Investigator Concerns

Investigators who have concerns or suggestions regarding Pennington Biomedical Research Center HRPP should convey them to the HRPP Director, Institutional Official or other responsible parties regarding the issue, when appropriate. The Institutional Official or HRPP Director will research the issue, and when deemed necessary, convene the parties involved to form a response for the Investigator or make necessary procedural or policy modifications, as warranted. In addition, the IRB Chair and/or the HRPP Director will be available to address Investigators' questions, concerns and suggestions.

13.0 Quality Improvement in the HRPP Program

13.1 Definitions

Quality Improvement: A process initiated to develop/enhance a practice or procedure and to institutionalize the practice or procedure.

Audit: A systematic review, inspection, or verification, typically conducted by an independent individual or group.

Routine (Not-for-Cause) **Review:** An assessment or examination of something (e.g., a practice or procedure) with the possibility or intention of instituting change if necessary.

Directed (For-Cause) **Audit/Review:** An audit of research and/or Investigators initiated at the request of the Institutional Review Board (IRB) or Institutional Official to obtain or verify information necessary to ensure compliance with regulations and Institutional requirements and to inform Institutional Officials and the IRB about decisions on the conduct of human subjects research and/or human subjects protection.

13.2 Scope of QI Program

The QI program focuses primarily on reviewing and monitoring of the activities, policies, procedures, and records for the following groups:

- Investigators and research staff participating in human subjects research
- IRB
- Individuals involved in HRPP education and outreach

13.3 QI Program Goals

The purpose of the HRPP QI program is to verify and promote the following:

- Protection of the rights, welfare, and safety of human subjects participating in research at the Pennington Biomedical Research Center
- Compliance with federal, state, and institutional requirements governing human subjects research
- Integrity of university research and HRPP activities
- Education and training of researchers, including administrators, Investigators, research staff, IRB members and faculty involved in human research
- Evaluation and follow-up of QI initiatives and corrective actions and implementation of new quality improvement activities
- Implement a QI plan that periodically assesses the compliance of the HRPP

13.4 Development and Review of QI Activities

The HRPP Director is responsible for drafting proposals for HRPP QI initiatives after review of the regulations, guidance, and findings from previous HRPP QI projects, in consultation with the IRB Chair.

13.5 Implementation of QI Activities

The HRPP Director is responsible for the implementation and communication of HRPP QI activities. Information and accompanying materials will be posted and made available on the HRPP website, as applicable. The Institutional Official or designee will set an effective date for implementation of new projects. When a HRPP QI initiative represents a significant change to existing processes or practices, the effective date will be set to allow for communication, including education and planning for operational changes.

13.6 QI Program Maintenance

The HRPP Director is responsible for maintaining the HRPP QI program. The HRPP Director will review program findings and ongoing HRPP QI initiatives as needed, at least annually. Specific findings from directed reviews will be forwarded to the IRB Chair, Pennington Biomedical Research Center HRPP Leadership Committee and/or the Institutional Official. Program initiatives will be developed (as described above) and/or updated as HRPP needs are recognized or changed.

13.7 QI Plan

13.7.1 Compliance Monitoring

The HRPP Staff conduct periodic and for-cause compliance audits to evaluate adherence to applicable federal regulations, state and local laws and Pennington Biomedical policies and procedures.

13.7.2 For-Cause Compliance Audits

For-Cause Compliance Audits may be conducted by the HRPP, IRB or other Institutional designees. These designees may be directed to conduct an assessment in response to a particular concern. Concerns that may prompt a for-cause audits include but are not limited to:

- Failure of routine audits
- Complaints or concerns initiated by a research participant, family member or research staff

- Reports of serious or repeated non-compliance
- Results of audits or monitoring conducted by the following sources: internal and external monitoring, NIH, and FDA audits

13.7.3 Periodic Compliance Audit of Protocols

Periodic Compliance Audits are conducted using systematic methods to assess Investigator and IRB compliance with federal regulations, local laws and Pennington Biomedical policies and procedures. A random selection of Investigator's human subject research records and consent forms are reviewed during these audits for compliance. The following information is reviewed and reported to the IRB:

- IRB file review – documentation of consent form modifications, adverse events, deviations, protocol modifications, monitor letters and continuing review documents
- Subject case file review – subject files contain proper documentation of adverse events, inclusion/exclusion criteria, concomitant medications, enrollment/termination, subject history, lab results, progress notes, physical assessments, drug/device information records, case report forms, source documents
- Consent/Assent/HIPAA for subjects – consent form in subject file, consent form signed and dated, IRB approved consent used, informed consent obtained prior to start of procedures, correct signatures obtained
- Protocol Adherence – inclusion/exclusion, study procedures performed as designated in protocol, approved concomitant therapy followed, protocol adherence requirements met
- Safety Monitoring – adverse events recorded appropriately, serious adverse events reported to the IRB
- Drug/Device Accountability – adequate record of receipt, dispensing/return records, drug used as per protocol, all authorized personnel appropriately signed for release of drug, IND drug record, administration of drug records present and appropriate

13.7.4 Reporting of Compliance Monitoring Results

Results of for-cause and periodic monitoring activities are documented and reported to the IRB, the PI and any other units within Pennington Biomedical as appropriate. The Institutional Official or designee are notified, if the results include non-compliance or other findings pertinent to Institutional Officials. The IRB will review these activities and decide the following:

- The periodic or for-cause audit shows only minor concerns, possible action(s) the IRB may consider:
    - The IRB may do nothing other than notify the PI of the findings
    - Ask the PI to formulate an action plan
    - The IRB may ask for re-education of the PI and staff
    - The IRB may mandate the study continued to be monitored to ensure process improvements were made.
- If the for-cause audit shows major concerns, the convened IRB will evaluate the concern to see if it meets the definition of non-compliance (see Policy 10 – Complaints and Compliance) and act according to the policy. Other actions the IRB may consider:
    - Ask the PI to formulate an action plan
    - The IRB may ask for re-education of the PI and staff
    - The IRB may mandate the study continued to be monitored to ensure process improvements were made.
    - Ask for modifications to the protocol/consent

13.7.5 Periodic Compliance Audit of IRB Minutes

Periodically the IRB completes an internal audit of the meeting minutes to ensure that all items listed in Policy 4 - Documentation and Records, are included in the IRB minutes. A report will be submitted to the convened IRB for discussion. Process improvements based on these audit results will be considered. Actions the IRB may consider:

- Change policies and procedures to address problems not documented in the minutes.
- Re-educate IRB Members and Staff on policies and procedures

13.7.6 Research Community Feedback Tracking

The HRPP office tracks comments, questions and issues received from participants to identify areas for potential improvement in the effectiveness of HRPP policies and procedures and for ensuring the protection of human subject research participants. The IRB staff will bring any serious and continuing complaints to the convened IRB for discussion. The IRB will rely on the policy and procedures defined in HRPP Policy 10 Complaints and Non-Compliance.

13.7.7 IRB Performance Metrics

The HRPP Director produces periodic metrics and analysis of the IRB operations and functions, including measurements of processing times and activity volumes for the IRB and for each protocol event.

13.7.8 Continuous Quality Improvement

Based on the results of the assessments and feedback received from communities served by the IRB, the HRPP office will work in partnership with the IRB and other components of the HRPP to:

- identify root causes of problems
- foster the development of solutions
- implement or recommend appropriate courses of action
- provide education and outreach programs
- evaluate effectiveness of solutions/outcomes

14.0 Participant Outreach Activities

14.1 Responsibility

It is the responsibility of the HRPP Director or designee to implement the procedures outlined below.

14.2 Outreach Resources and Educational Materials

In order to involve and inform current and future research participants in accordance with the Belmont principle of Respect for Persons, Pennington Biomedical Research Center HRPP maintains a “Research Participants” page on the HRPP website. This page provides resources for research participants. In addition, research participants are invited via the website to contact HRPP/IRB staff to provide feedback and/or obtain information about human subjects research and HRPP activities.

The following resources are provided to participants:

- Opportunity to submit concerns, trial information and receive feedback.
- Participant Brochure
- Links to government websites (e.g., OHRP, FDA, NIH)

14.3 Questions, Concerns and Complaints

All complaints, concerns and questions received by the IRB from any individual through the Concerns and Complaints Form or any form of communication will be acknowledged and forwarded to the appropriate individual within the Institution for handling and follow-up. While the IRB expects a prompt resolution, the time frame is dependent on the complexity of the complaint or concern.

Contact information for reporting complaints or concerns is provided in the informed consent, participant brochure and the HRPP website.

14.4 Periodic Evaluation

Pennington Biomedical Research Center periodically evaluates its outreach activities and makes changes when appropriate. These evaluations take place in an informal, ongoing manner. All IRB members, IRB Chair, IRB Staff and HRPP Staff will report both positive and negative feedback regarding outreach activities to the HRPP Director who will track the input and suggest changes be made to improve outreach activities. The HRPP Director will summarize the material annually in order to formally evaluate its outreach activities and determine:

1. The specific community outreach activities being used; and
2. Whether or not these community outreach activities have an evaluative component, and if so what, if any, changes in the outreach activities have resulted from these.

15.0 Research Funded by the Department of Defense

The following considerations apply to human subjects research supported by a Department of Defense component through a contract, grant, or other arrangement.

A Department of Defense component is a military department, defense agency, DOD field activity, or organization within the Office of the Secretary of Defense. DOD components include but may not be limited to the following: Department of Defense, Army, National Guard, Navy, Air Force, Marines, and U.S. Army Corps of Engineers.

15.1 Definitions as Defined by DOD

DOD subjects: This includes any person captured, detained, held, or otherwise under the control of DOD personnel (military, civilian, or contractor employee). Such persons include: Enemy Combatant, Lawful Enemy Combatant, Unlawful Enemy Combatant, Retained Person, and Civilian Internee. Such persons do not include personnel of the DOD being held for law enforcement purposes. It does not include persons being held primarily for law enforcement purposes, except where the United States is the occupying power. This prohibition does not apply to activities covered by investigational new drug or investigational device provisions. This prohibition does not apply to activities covered by investigational new drug or investigational device provisions the purpose of diagnosis or treatment of a medical condition in a patient. Such treatment (e.g., an investigational new drug) may be offered to detainees with the detainees' informed consent when the medical products are subject to FDA regulations investigational new drugs or investigational medical devices, and only when the same product would be offered to members of the U.S. Military Services in the same location for the same medical condition and only when consistent with established medical practice involving investigational drugs and devices.

DOD Research Involving Interventions or Interactions with Subjects: Research involving a human being as a research subject is an activity, for research purposes, where there is an intervention or interaction with a living individual for the primary purpose of obtaining data regarding the effect of the intervention or interaction. Research involving a human being as a research subject is a subset of research involving human subjects. This definition does not include exempt research involving human subjects.

DOD Research Monitor: The research monitor may be identified by an Investigator or appointed by an IRB or IO for research involving human subjects determined to involve minimal risk. There may be more than one research monitor (e.g., if different skills or experiences are necessary). The monitor may be an ombudsman or a member of the data safety monitoring board. The Heads of the OSD and DOD Components may waive

the requirement to have a research monitor on a case-by-case basis when the inclusion of a research monitor is not necessary to provide additional protections for human subjects. This waiver authority may be delegated to a DOD official, as described in the Component's HRPP management plan, but not at or below the position of the institution's DOD IO.

DOD Ombudsman: independent, impartial resource that provides DOD employees worldwide with a safe harbor for informal and confidential dispute resolution.

DOD Minimal Risk: Minimal risk is based on the phrase "ordinarily encountered in daily life or during the performance of routine physical or physiological examination or tests"; minimal risk shall not be interpreted to include the inherent risks certain categories of human subjects face in their everyday life. For example, the risks imposed in research involving human subjects focused on a special population should not be evaluated against the inherent risks encountered in their work environment (e.g., emergency responder, pilot, soldier in a combat zone) or having a medical condition (e.g., frequent medical tests or constant pain.)

The definition of minimal risk in 32 CFR 219 does not include the inherent occupational risks that certain participants face in their everyday life, such as those:

- Encountered by Service members, law enforcement, or first responders while on duty.
- Resulting from or associated with high-risk behaviors or pursuits.
- Experienced by individuals whose medical conditions involve frequent tests or constant pain.

15.2 Policy

15.2.1 Criteria for Approval Specific to DOD

- When appropriate, research protocols must be reviewed and approved by the IRB prior to the Department of Defense approval. Consult with the Department of Defense funding component to see whether this is a requirement.
- Service members must follow their command policies regarding the requirement to obtain command permission to participate in research involving human subjects while on-duty or off-duty.
- There may be specific educational requirements or certification required by DOD above the educational requirements required by the institution. It is the Principal Investigator's responsibility to ensure that research staff has completed all appropriate educational requirements as mandated by DOD policy. The Department of Defense component may evaluate the education policies to ensure

the personnel are qualified to perform the research, based on the complexity and risk of the research.

- The disclosure regarding provisions for research-related injury follows the requirements of the DOD component. The PI is responsible for informing the IRB, in writing, if there are any additional requirements from the DOD Component regarding the provision of care in the case of a research-related injury.
- When conducting multisite research, a formal agreement is required to specify the roles and responsibilities of each party including a Statement of Work (SOW) and specific assignment of responsibilities.
- Surveys performed on Department of Defense personnel must be submitted, reviewed, and approved by the Department of Defense after the research protocol is reviewed and approved by the IRB. When a survey crosses DoD Components, additional review is required.
- If consent is to be obtained from the research subjects' legal representative, the research must intend to benefit the individual participant.
- The determination that research is intended to be beneficial to the individual research subject must be made by an IRB.
- When Investigators are following ICH-GCP (E6) guidelines, Investigators and research staff must provide all the disclosures and follow the requirements pertaining to consent covered by ICH-GCP (E6).
- The Investigator and research staff are aware of the specific DOD requirements and have been educated about these requirements.
- The research does NOT involve prisoners of war or detainees as subjects.
- The research does NOT involve classified research.
- The research does NOT involve the testing of chemical or biological agents.
- If an IRB at a non-DoD institution reviews DoD-supported research, the IRB must consider the scientific merit of the research, including consideration of feasibility of study completion.
- The IRB may rely on outside experts to provide an evaluation of the scientific merit.
- If the research involves DoD-affiliated personnel as participants, in addition to the basic and required consent disclosures, consent documents must include:
    - If the research involves risks to their fitness for duty (e.g., health, availability to perform job, data breach), the informed consent document (ICD) must inform DoD- affiliated personnel about these risks and that they should seek command or Component guidance before participating.
    - If applicable, a statement of potential risks for the revocation of clearance, credentials, or other privileged access or duty.

- Consent documents for all DoD-conducted and DoD- supported research must include:
    - A statement that the DoD or a DoD organization is funding the study.
    - A statement that representatives of the DoD are authorized to review research records.
- For greater than minimal risk research, consent documents must include the disclosure that participants may, for the duration of the study, be eligible for health care services for research-related injuries at a military treatment facility, and this eligibility for health care services extends beyond participants' participation in the study to such time after the study has ended.
- Written materials must document how institutions will care for participants with research-related injuries, including injuries that are the direct result of activities performed by DoD- affiliated personnel in studies that are collaborative with a non-DoD institution.
- For greater than minimal risk research involving DoD-personnel, when recruitment and consent occurs in a group setting, the IRB must appoint an ombudsperson. The ombudsperson:
- Must not have a conflict of interest with the research or be a part of the research team.
- Must be present during the HSR recruitment, monitoring that the recruitment and informed consent explain that participation is voluntary and that the information provided about the research is consistent with the IRB- approved script and materials, including digitally provided materials.
- Should be available to address DoD-affiliated personnel's concerns about participation.
- If the research involves a "human being as an experimental subject", as defined by DoDI 3216.02, and is supported by DoD-appropriated funds, informed consent must be obtained from the participant in advance, in accordance with 10 USC 980.
- If the participant is unable to provide informed consent and consent will be obtained in advance from the participant's legal representative, the research must be intended to benefit the individual participants.
- Civilian researchers attempting to access military volunteers should seek collaboration with a military researcher familiar with service-specific requirements.

15.2.1.1 The DoD Component

The DoD Component must conduct an appropriate administrative review of DoD-conducted and/or DoD-supported research involving human

participants if the research meets certain criteria. The DoD Component administrative review must be conducted before the research involving human participants can begin to ensure compliance with all applicable regulations and policies. DoD Component administrative reviews must be conducted when:

- Human participant's research is conducted in a foreign country, unless conducted by a DoD overseas institution, or only involves DoD-affiliated personnel who are US citizens. **PBRC does not do foreign research.**
- The research requires a waiver of informed consent pursuant to 10 USC 980, Subsection (b)
- The research is fetal research, as described in 42 USC 289g-289g-2. Large scale genomic data is collected from DoD-affiliated personnel.
- The research constitutes classified research involving human participants, as defined by DoDI 3216.02.
- The research is required to be approved by the DOHRP, in accordance with DoDI 3216.02.
- DoD institutions collaborating with non-DoD institutions may rely on a collaborating non-DoD institution's IRB if the following conditions are met:
    - Each institution engaged in non-exempt human participant research must have a current federal assurance of compliance.
    - The non-DoD institution's IRB is registered in accordance with 45 CFR 46, Subpart E.
    - The DoD institution, non-DoD institution, and the non-DoD institution's IRB have a written agreement defining the responsibilities and authorities of each organization in complying with all legal requirements. This agreement must specify that the non-DoD IRB will apply the DoD requirements specified in DoDI 3216.02.
    - If the research constitutes classified human participant research, the Component Office for Human Research Protections (COHRP), on behalf of the Component's Senior Designated Official, must approve the agreement to rely on the non-DoD institution's IRB.

15.2.2 DOD Criteria for Waiver of Consent

- If non-exempt research is supported by DoD-appropriated funds and involves experimental subjects as defined in DODI 3216.02, consent must be obtained in advance, in accordance with 10 USC 980.
    - An IRB may waive or alter some elements of informed consent for research involving human beings as experimental subjects, as long as it preserves the informed consent of the participant or the participant's legal representative (i.e., the consent indicates that participation in the research is voluntary and the participant/representative is informed of research risks).
- The DOHRP may waive the requirements for prospective consent for research involving human beings as experimental subjects when all of the following are met:
    - The research is necessary to advance the development of a medical product for the Military Services.
    - The research may directly benefit the individual experimental subject.
    - The research is conducted in compliance with all other applicable laws and regulations.

15.2.3 DOD Policy Regarding Payment for Research

- Employees of the Department of Defense (including temporary, part-time, and intermittent appointments) may not be able to legally accept payments to participate in research and should check with their supervisor before accepting such payments. Employees of the Department of Defense cannot be paid for conducting research while on active duty.
- Military personnel will not be paid for research conducted while on duty; however, the personnel can be compensated if involved in the research while not on duty.
- Although federal personnel participating as human subjects in DOD-conducted research while on duty may be compensated up to $50 for each blood draw for scientific and research purposes in connection with the care of any person entitled to treatment at government expense, this IRB allows no such compensation when compensation is otherwise prohibited.
- Military personnel can participate in research off-duty; however, they cannot be paid from federal funds for research conducted while off duty.

- Non-Federal persons may be compensated for research participation other than blood draws in a reasonable amount as approved by the IRB according to local prevailing rates and the nature of the research.

15.2.4 DOD Policy Regarding Recruitment

- Superiors will not influence the decisions of their subordinates regarding participation in research.
- Superiors will not be present at the time of recruitment and consent. When applicable, the superiors so excluded shall be afforded the opportunity to participate as human subjects in a separate recruitment session.
- When recruitment involves a percentage of a unit, an ombudsman, who is independent of both the proposed research as well as the unit must be present to monitor that the voluntary nature of the individual participants is adequately stressed and that the information provided about the research is adequate and correct.
- Research involving minimal risk: The IRB has discussed and determined whether to appoint an ombudsman based in part on the subject population, the consent process, and the recruitment strategy.
- Research involving greater than minimal risk: The IRB has appointed an ombudsman who is unassociated to the research and will be present during the recruitment to monitor that voluntary participation is clearly and adequately stressed and that information provided about the research is clear, adequate, and accurate. The ombudsman may also be the research monitor.
- DoD-affiliated personnel, military and civilian supervisors, officers, and others in the chain of command:
    - Are prohibited from influencing their subordinates to participate in research involving human participants.
    - Must not be present at any human participant recruitment sessions or during the consent process for DoD-affiliated personnel.
    - May participate in separate human participant research recruitment sessions.
- For greater than minimal risk research involving DoD-personnel, when recruitment and consent occurs in a group setting, the IRB must appoint an ombudsperson. The ombudsperson:
    - Must not have a conflict of interest with the research or be a part of the research team.
    - Must be present during the HSR recruitment, monitoring that the recruitment and informed consent explain that participation is voluntary and that the information provided about the research is consistent with the IRB- approved script and materials, including digitally provided materials.

- Should be available to address DoD-affiliated personnel's concerns about participation.

- In conducting or supporting clinical research, the Secretary of Defense shall ensure that:
  - Women who are members of the Armed Forces are included as participants in each project of such research.
  - Members of minority groups who are members of the Armed Forces are included as participants of such research.
  - The Secretary of Defense may waive these requirements regarding women and members of minority groups with respect to a project of clinical research if the Secretary determines that the inclusion, as participants in the project, of women and members of minority groups, respectively:
    - Is inappropriate with respect to the health of the participants,
    - Is inappropriate with respect to the purpose of the research, or
    - Is inappropriate under such other circumstances as the Secretary of Defense may designate.

15.2.5 DOD Research with impaired decision-making capacity individuals

- If the research involves interventions or interactions with individuals with impaired decision-making capacity, there must be an anticipated direct benefit to the subject.

15.2.6 DOD Research Involving Pregnant Women, Prisoners and Children

- Research involving pregnant women, prisoners, and children are subject to the DHHS Subparts B, C. and D.
  - Research involving pregnant women, prisoners, and children are subject to the DHHS Subparts B, C, and D, except where modified by DoDI 3216.02:
    - Research or experimentation may not be conducted, in the United States or in any other country, on a nonviable living human fetus ex utero or a living human fetus ex utero for whom viability has not been ascertained unless the research or experimentation:
      - May enhance the well-being or meet the health needs of the fetus or enhance the probability of its survival to viability; or
      - Will pose no added risk of suffering, injury, or death to the fetus and the purpose of the research or experimentation is the development of important biomedical knowledge

which cannot be obtained by other means.
    - The risk standard must be the same for fetuses which are intended to be aborted and fetuses which are intended to be carried to term.
- For human participant research that would not otherwise be approved but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates, DoD organizations must demonstrate to the senior designated official that the IRB has fulfilled its duties in accordance with Subpart B. Before human participant research activities may begin, the Senior Designated Official must receive explicit written approval from the DoD Office for Human Research Protections.
- When a previously enrolled human participant becomes a prisoner, and the protocol has not been reviewed and approved by the IRB in accordance with Subpart C, the key researcher must promptly notify the IRB.
    - For DoD-conducted research, the human protections director must notify the Component Office of Human Research Protections.
    - For DoD-supported research, the non-DoD organization must notify the DoD HRPO and other federal agencies.
    - The DOHRP must concur with the IRB before the participant can continue to participate while a prisoner.
- Service members and DoD-affiliated personnel are considered to be vulnerable to coercion and undue influence by the DoD due to the nature of the command structure of the organization. Therefore, additional protections for DoD- affiliated personnel are required, as follows:
    - If the research involves DoD-affiliated personnel as participants and if the research includes any risks to their fitness for duty (e.g., health, availability to perform job, data breach), the informed consent document must inform DoD-affiliated personnel about these risks and that they should seek command or Component guidance before participating.
    - If the research involves DoD-affiliated personnel, the key researcher must receive command or Component approval to execute the research.
    - Military and civilian supervisors, officers, and others in the chain of command are prohibited from influencing their subordinates to participate in research.
    - Military and civilian supervisors, officers, and others in the chain of command must not be present at any participant recruitment sessions or during the consent process for DoD-affiliated personnel. Excluded supervisors or those in the

chain of command may participate in separate recruitment sessions, if applicable.

- Service members and all Reserve Component and National Guard members in a federal duty status are considered to be adults. If a Service member, Reserve Component or National Guard member in federal duty status, student at a Service Academy, or trainee is under 18 years of age, the IRB must carefully consider the HSR recruitment process and the necessity of including such member as a human participant.
- In order to approve research involving DoD-affiliated personnel, the IRB or HRPO must determine whether the following requirements have been satisfied:
    - The consent documentation must include, if applicable, potential risks for revocation of clearance, credentials, or other privileged access or duty.

- For research involving recruitment of DoD-affiliated personnel in research determined to be greater than minimal risk, and when recruitment occurs in a group setting, the IRB must appoint an ombudsperson. The ombudsperson:
    - Must not have a conflict of interest with the research or be a part of the research team.
    - Must be present during the recruitment, monitoring that the recruitment and informed consent explain that participation is voluntary and that the information provided about the research is consistent with the IRB- approved script and materials, including digitally provided materials.
    - Should be available to address DoD-affiliated personnel's concerns about participation.
- Compensation to DoD-affiliated personnel for participation in research while on duty is prohibited in accordance with 5 USC, with particular reference to Subparts G and H, with some exceptions for purposes consistent with 24 USC 30.
- Research involving large-scale genomic data from DoD-affiliated personal requires additional protections:
    - The disclosure of DoD-affiliated personnel's genomic data may pose a risk to national security; accordingly, written materials must describe administrative, technical, and physical safeguards commensurate with risk, including the secondary use or sharing of de- identified data or specimens.
    - All research involving large-scale genomic data collected from DoD-affiliated personnel must have a certificate of confidentiality.
    - Research involving large-scale genomic data collected from DoD-affiliated personnel is subject to DoD Component

security review to ensure the adequacy of the proposed administrative, technical, and physical safeguards, including the secondary use or sharing of de-identified data or specimens.

15.2.6.1 DOD Research – Subpart B – Research with Pregnant Women and Fetuses

- For purposes of applying Subpart B, the phrase "biomedical knowledge" shall be replaced with "generalizable knowledge."
- The applicability of Subpart B is limited to research involving pregnant women as participants in research that is more than minimal risk and included interventions or invasive procedures to the woman or the fetus or involving fetuses or neonates as participants.
- Fetal research must comply with the US Code Title 42, Chapter 6A, Subchapter III, Part H, 289g.

15.2.6.2 DOD Research – Subpart D – Research with Children

- Research involving children cannot be exempt.

15.2.7 DOD Research Involving More Than Minimal Risk

15.2.7.1 DOD Research – Research Monitor

- A research monitor is not required. Researchers may remove the requirement for a research monitor from existing open studies through a modification approved by an IRB.

15.2.8 DOD Research – Non-U.S. Citizens

- If the research involves human subjects who are not U.S. citizens or personnel of the DOD, and is conducted outside the United States, its territories, and its possessions, the IRB will verify:

    - The permission of the host country has been obtained.
    - The laws, customs, and practices of the host country and the United States will be followed.
    - An ethics review by the host country, or local IRB with host country representation, will take place.

15.2.9 DOD Research – Non-Compliance

See the following regarding non-compliance for Department of Defense research:

- Records maintained that document compliance or non-compliance with Department of Defense requirements shall be made accessible for inspection and copying by representatives of the Department of Defense at reasonable times and in a reasonable manner as determined by the supporting DOD component.

15.2.10 DOD Research – Additional Reporting Requirements by Investigator to DOD

- The following shall be promptly reported (within 30 days) to the Department of Defense Human Research Protections Officer by the Investigator:
    - When significant changes to the research protocol are approved by the IRB.
    - Decreased benefit or increased risk to participants is greater than minimal risk research.
    - Addition of vulnerable populations as participants.
    - Addition of DoD-affiliated personnel as participants.
    - The results of the IRB continuing review.
    - Change of reviewing IRB.
    - When a previously enrolled human participant becomes pregnant, or when the researcher learns that a previously enrolled human participant is pregnant, and the protocol was not reviewed and approved by the IRB in accordance with Subpart B.
    - When a previously enrolled human participant becomes incarcerated, or when the researcher learns that a previously enrolled human participant is incarcerated, and the protocol was not reviewed and approved by the IRB in accordance with Subpart C.
    - A DoD-supported study's closure.
    - When the organization is notified by any Federal department, agency or national organization that any part of the HRPP is under investigation for cause involving a DOD-supported research protocol.
    - Any unanticipated problems involving risks to participants or others for any DoD-supported research must be promptly (no longer than within five days) reported to the DoD Office for Human Research Protections.

15.2.11 DOD Research – Additional Reporting Requirements by IRB

- The following must be promptly reported to the Directorate of Human Research Protections (DOHRP):

- Reports of audits of DoD-conducted or DoD-supported human participant research by another federal or state agency, official governing body of a Native American or Alaskan native tribe, other official entity, or foreign government, within 5 business days of discovering that such audit reports exist.
- Allegations of serious or continuing noncompliance related to HSR that are substantiated by investigation, and subsequent actions taken based on the findings, within five business days of completion of the report.
- Unanticipated problems involving risks to human participants or others and subsequent actions taken based on the findings, within five business days of completion of the report.
- Any suspension or termination of DoD-supported research must be promptly (no longer than within five days) reported to the DoD Office for Human Research Protections (DOHRP).
- Substantiated allegations related to classified HSR must be reported immediately (less than five days) to the DOHRP.

15.2.12 DOD Research – Certificate of Confidentiality

- When following DoD requirements:
    - Data or information acquired by the DoD Component under a pledge of confidentiality for exclusively statistical purposes must be used exclusively for statistical purposes and may not be disclosed in identifiable form for any other purpose, except with the informed consent of the respondent.
    - All studies involving large scale genomic data collected on/from DoD-affiliated personnel will apply an HHS Certificate of Confidentiality.

16.0 Research Conducted by the Department of Education

Additional regulatory considerations are required for human research that is funded by the U.S. Department of Education (ED), and/or is conducted in institutions that receive ED funding.

For research funded by the National Institute on Disability and Rehabilitation Research, when an IRB reviews research that purposefully requires inclusion of children with disabilities or individuals with mental disabilities as research participants, the IRB must include at least one person primarily concerned with the welfare of these research participants. 34 CFR 350.4(c) and 356.3(c)

16.1 FERPA

The Family Educational Rights and Privacy Act (FERPA) of 1974 (as amended) is a federal law that sets forth requirements for the protection of privacy of students' educational records. This policy addresses the applicability of FERPA to human subject research reviewed by the Pennington Biomedical Research Center Institutional Review Board (IRB).

16.2 FERPA Definitions

Directory information: means information contained in an education record of a student that would not generally be considered harmful or an invasion of privacy if disclosed.

a) Directory information includes, but is not limited to, the student's name; address; telephone listing; electronic mail address; photograph; date and place of birth; major field of study; grade level; enrollment status (e.g., undergraduate or graduate, full-time or part-time); dates of attendance; participation in officially recognized activities and sports; weight and height of members of athletic teams; degrees, honors and awards received; and the most recent educational agency or institution attended.
b) Directory information does not include a student's
    1. Social security number; or
    2. Student identification (ID) number, except as provided in paragraph (c) of this section.
c) Directory information includes a student ID number, user ID, or other unique personal identifier used by the student for purposes of accessing or communicating in electronic systems, but only if the identifier cannot be used to gain access to education records except when used in conjunction with one or more factors that authenticate the user's identity, such as a personal

identification number (PIN), password, or other factor known or possessed only by the authorized user.

Disclosure: means to permit access to or the release, transfer, or other communication of personally identifiable information contained in education records by any means, including oral, written, or electronic means, to any party except the party identified as the party that provided or created the record.

Education records:

a) The term means those records that are:
    1. Directly related to a student; and
    2. Maintained by an educational agency or institution or by a party acting for the agency or institution.

b) The term does not include:
    1. Records that are kept in the sole possession of the maker, are used only as a personal memory aid, and are not accessible or revealed to any other person except a temporary substitute for the maker of the record.
    2. Records of the law enforcement unit of an educational agency or institution, subject to the provisions of 99.8.
    3. Records relating to an individual who is employed by an educational agency or institution, that:
        - Are made and maintained in the normal course of business;
        - Relate exclusively to the individual in that individual's capacity as an employee; and
        - Are not available for use for any other purpose.
            - Records relating to an individual in attendance at the agency or institution who is employed as a result of his or her status as a student are education records and not excepted under this definition.
    4. Records on a student who is 18 years of age or older, or is attending an institution of postsecondary education, that are:
        - Made or maintained by a physician, psychiatrist, psychologist, or other recognized professional or paraprofessional acting in his or her professional capacity or assisting in a paraprofessional capacity;
        - Made, maintained, or used only in connection with treatment of the student; and
        - Disclosed only to individuals providing the treatment. For the purpose of this definition, ''treatment'' does not include remedial

educational activities or activities that are part of the program of instruction at the agency or institution; and

5. Records created or received by an educational agency or institution after an individual is no longer a student in attendance and that are not directly related to the individual's attendance as a student.
6. Grades on peer-graded papers before they are collected and recorded by a teacher.

Educational agency or institution means any public or private agency or institution to which this part applies under 99.1(a).

Eligible student means a student who has reached 18 years of age or is attending an institution of postsecondary education.

Parent means a parent of a student and includes a natural parent, a guardian, or an individual acting as a parent in the absence of a parent or a guardian.

Personally Identifiable Information. The term includes, but is not limited to:

a) The student's name;
b) The name of the student's parent or other family members;
c) The address of the student or student's family;
d) A personal identifier, such as the student's social security number, student number, or biometric record

16.3 FERPA Policy

FERPA applies to educational agencies or institutions to which funds have been made available under any program administered by the Secretary of the U.S. Department of Education if the institution provides educational services or instruction to students and is authorized to direct and control public elementary, secondary, or post-secondary educational institutions. 34 CFR 99.1(a). Funds include those provided to the institution by grant, cooperative agreement, contract, subgrant, or subcontract or if funds are provided to the students attending the institution. If there is a question about the applicability of FERPA to an educational institution, 34 CFR 99.1 should be reviewed.

The education records protected by FERPA are those records that directly related to a student and are maintained by an educational agency or institution or by a party acting for the agency or institution. 34 CFR 99.3. When FERPA is applicable, consent from the parent or student is required in order for the educational institution to disclose the education record or the disclosure must meet an exception criteria found in 34 CFR

99.31. Such disclosures may be requested to obtain student records as part of a human subject research study.
The disclosure must be to an institution (Pennington Biomedical Research Center) conducting studies for, or on behalf of, educational agencies or institutions to:

a. Develop, validate, or administer predictive tests;
b. Administer student aid programs; or
c. Improve instruction

Unless the request meets an exception in 34 CFR 39.31, signed and dated written consent must be obtained from the parent or eligible student before the educational institution discloses the personally identifiable information. 34 CFR 99.30(a). Written consent must include the following elements (34 CFR 90.30(b)):

a. Specify the records that may be disclosed
b. State the purpose of the disclosure; and
c. Identify the party or class of parties to whom the disclosure may be made

If the request involves an exception to parental permission or student consent, the request must meet an exception provided in 34 CFR 99.31(a). The exceptions relevant to research include 34 CFR 99.31(a)(6) or 34 CFR 99.31(11).

a. The following requirements apply to this exception:
The exception under 34 CFR 99.31(11) permits educational institutions or agencies to release “directory information” from students without consent so long as the conditions under 34 CFR 99.37 are met. A researcher may receive directory information from an educational institution without student or parental consent as required by FERPA. If a student’s social security number or other non-directory information is used alone or combined with other data elements to identify or help identify the student or the student’s records, informed consent must be obtained. 34 CFR 99.37(d)
    1) In order for the student records to be disclosed, the researcher on behalf of Pennington Biomedical Research Center, must enter into a written agreement with the educational agency or institution. The written agreement must contain the following elements (34 CFR 99.31(6)(ii)(C)):
        a. Specifies the purpose, scope, and duration of the study or studies and the information to be disclosed
        b. Requires the organization to use personally identifiable information from education records only to meet the purpose or purposes of the study as stated in the written agreement
        c. Requires the organization to conduct the study in a manner that does not permit personal identification of parents and students by anyone other than representatives of the organization with legitimate interests

   d. Requires the organization to destroy or return to the educational agency or institution all personally identifiable information when the information is no longer needed for the purposes for which the study was conducted and specifies the time period in which the information must be returned or destroyed
2) Once the information is disclosed to the researchers, the limitations outlined in the written agreement on use of the student data must be followed. 34 CFR 99.31(6)(ii).

A school district or postsecondary institution that uses the exceptions to parental/student consent to release student records for research is required to enter into a written agreement with the organization or researcher conducting the research that specifies:

- The determination of the exception.
- That information from education records may only be used to meet the purposes of the study stated in the written agreement and must contain the current requirements in 34 CFR 99.31(a)(6) on re-disclosure and destruction of information.

Education records may be released without consent under FERPA if all personally identifiable information has been removed including:

- Student's name and other direct personal identifiers, such as the student's social security number or student number.

- Indirect identifiers, such as the name of the student's parent or other family members; the student's or family's address, and personal characteristics or other information that would make the student's identity easily traceable; date and place of birth and mother's maiden name.

- Biometric records, including one or more measurable biological or behavioral characteristics that can be used for automated recognition of an individual, including fingerprints, retina and iris patterns, voiceprints, DNA sequence, facial characteristics, and handwriting.

- Other information that, alone or in combination, is linked or linkable to a specific student that would allow a reasonable person in the school community, who does not have personal knowledge of the relevant circumstances, to identify the student with reasonable certainty.

16.4 Protections of Pupil Rights Amendment (PPRA)

PPRA affords parents certain rights regarding theconduct of surveys, collection and use of information for marketing purposes, and certain physical exams. These include the right to:

- If the survey is funded in whole or in part by a program of the U.S. Department of Education (ED), no student shall be required, as part of any research project, to submit without prior consent to surveys, psychiatric examination, testing, or treatment, or to psychological examination, testing, or treatment, in which the primary purpose is to reveal information concerning on or more of the following:
  1. Political affiliations or beliefs of the student or student's parent;
  2. Mental or psychological problems of the student or student's family;
  3. Sex behavior or attitudes;
  4. Illegal, anti-social, self-incriminating, or demeaning behavior;
  5. Critical appraisals of others with whom respondents have close family relationships;
  6. Legally recognized privileged relationships, such as with lawyers, doctors, or ministers;
  7. Religious practices, affiliations, or beliefs of the student or parents; or
  8. Income, other than as required by law to determine program eligibility.

- Receive notice and an opportunity to opt a student out of
  1. Any other protected information survey, regardless of funding;
  2. Any non-emergency, invasive physical exam or screening required as a condition of attendance, administered by the school or its agent, and not necessary to protect the immediate health and safety of a student, except for hearing, vision, or scoliosis screenings, or any physical exam or screening permitted or required under State law; and
  3. Activities involving collection, disclosure, or use of personal information obtained from students for marketing or to sell or otherwise distribute the information to others.

- Inspect upon request and before administration or use
  1. Protected information surveys of students;
  2. Instruments used to collect personal information from students for any of the above marketing, sales, or other distribution purposes; and
  3. Instructional material used as part of the educational curriculum.

These rights transfer from the parents to a student who is 18 years old or an emancipated minor under State law.

16.4.1 Investigator Responsibilities

Investigators must provide an assurance letter from each school in which the research will be conducted stating that the school complies with the Family Educational Rights and Privacy Act (FERPA) and the Protections of Pupil Rights Amendment (PPRA).

Investigators must provide a copy of all surveys and instructional material used in the research. Parents of children involved in the research must be able to inspect these materials upon request within a reasonable amount of time.

Investigators must ensure the school in which the research is being conducted must have policies regarding the administration of physical examinations or screenings that the school may administer to students.

16.5 IRB Review of Department of Education Research

Requests for use in research must be submitted to the IRB. The IRB will evaluate such requests, including any exceptions to parental permission and student consent, for compliance with FERPA and PPRA requirements.

a. An educational agency or institution may disclose education records or information from education records without consent if the disclosure is after the removal of all personally identifiable information, provided that the educational agency/institution (or other party that received the information or education records) has made a reasonable determination that a student's identity is not personally identifiable, whether through single or multiple releases, and taking into account other reasonably available information.
b. All instructional material--including teachers' manuals, films, tapes, or other supplementary instructional material--which will be used in connection with any research or experimentation program or project must be available for inspection by the parents or guardians of the children engaged in such research.
c. Research or experimentation program or project means any program or project in any research that is designed to explore or develop new or unproven teaching methods or techniques.

17.0 Community-Based Participatory Research

In some instances, the design and implementation of research can be enhanced when individuals from the community in which the research will be conducted are involved in the design, conduct, and analysis of data from the research. This can occur for an individual study or group of studies. Pennington Biomedical Research Center facilitates the involvement of community members by supporting researchers who wish to conduct community-based participatory research or other types of research that involve community members.

17.1 Considerations for Investigators Involved in Community-Based Research

- Does the community partner have an IRB and/or approval process?
- If community partners are involved in research activities, are the partners considered "engaged" under federal law. If the community partners are considered engaged, they must complete all mandatory education criteria outlined in Pennington Biomedical Research Center Institutional Policy 106.00.
- Consent forms should be reviewed to ensure the reading level is appropriate for the planned participants. An 8th grade reading level is suggested.
- The IRB will need to know how the data will be shared with the community partners.

17.2 IRB Review of Community-Based Research

The IRB office follows the federal regulations and established policies and procedures when reviewing Community-Based Research protocols.

The following detail the IRB review of community-based research:

- The IRB will include members with experience conducting community research.
- Under Pennington Biomedical policies and procedures, the IRB may contact a consultant to review any research study where additional expertise is required, including community-based research.
- The IRB will review the research with the same policies and procedures outlined in the HRPP policies and procedures manual Policy 3 – IRB Review.

17.3 Additional Consideration in the IRB Review of Community-Based Research

- Does the community partner have an IRB and/or approval process?
- If community partners are involved in research activities, are the partners considered “engaged” under federal law. If the community partners are considered engaged, they must complete all mandatory education criteria outlined in Pennington Biomedical Research Center Institutional Policy 106.00.
- Consent forms should be reviewed to ensure the reading level is appropriate for the planned participants. An 8th grade reading level is suggested.
- If any of the research will take place in participants’ homes, the investigator must address issues of mandated reporting under state laws, if sensitive questions are being asked.
- Issues of privacy, confidentiality and coercion must be addressed.

17.4 Involving Community Members in the Research Process

- To understand the potential role of racial and cultural differences among population groups and how such differences may impact research study design, analysis and interpretation, the institution, its researchers, and administrative departments foster relationships with various community partners, churches, community centers, and local organizations to determine how best to engage diverse populations in research. Free glucose screening, diabetes prevention education, and advertisements (e.g., local newspapers, billboards, and social media platforms) directly target these populations.
- To help researchers identify relevant community members to involve in the research process, PBRC Recruitment Department maintains relationships with local community resources with expertise in hard-to-reach populations.
- Through partnerships with the Baton Rouge Mayor’s office and local organizations, the institution provides resources and expertise to hard-to-reach populations.
- The institution’s Research Computing and Recruitment Departments maintain listservs and various data on study volunteers and community demographics that aid investigators as they plan research proposals.
- The institution evaluates the racial or ethnic demographic characteristics of subjects enrolled in research to evaluate whether participation in research reflects the demographics of the community, when appropriate. This information is documented in the facilities report and is decimated to the Associate Executive Directors with approval by the Executive Director.

- The Community Members of the IRB, who are unaffiliated with the institution and can be scientific or nonscientific, are expected to provide input regarding their individual knowledge about the local community and be willing to discuss issues and research from that perspective.

18.0 Electronic Signatures and Electronic Records in IRBManager Software

18.1 Summary Policy

21 CFR Part 11 has been in effect since August 1997 and establishes certain requirements of the Food and Drug Administration (FDA). 21 CFR 11 covers two issues: electronic records and electronic signatures.

18.2 Electronic Records and Signatures

18.2.1 Identification controls and limiting of system access to authorized individuals

The access to the system used for electronic IRB submissions and reviews (IRBManager) will be limited to authorized users. Each IRBManager user must have a registered account with a unique name and password and a specified level of system access/authority. Only IRB staff is authorized to enable log-in of authorized users. Before access is granted, the user must sign an attestation agreeing that the individual user is accountable and responsible for actions initiated under their electronic signature, and that the user will not disclose their username and password to anyone else. Before enabling access, an IRB staff member will ensure that the attestation has been signed by the user. In addition, the IRB staff will assign the appropriate access level (IRB member, investigator, etc.) based on the user status and document that assignment on the attestation form.

18.2.2 Determination that persons who develop, maintain or use the electronic record/electronic signature systems have the education, training, and experience to perform their assigned tasks

In addition, the attestation requires a certification that a potential system user has completed training on IRBManager, either by attending an IRB provided training session or reviewing the on-line IRB training modules.

18.2.3 Establishment of written policies that hold individuals responsible and accountable for actions initiated under their electronic signatures

The HRPP Office notes that “Only the individual owner of an account is authorized to use that account. Providing passwords or in any way permitting or making it possible for anyone other than the authorized owner of the account to use computer resources is not authorized and may be a violation of Pennington Biomedical Policy 603.00.”

In addition, this policy addresses this requirement with regard to electronic signatures.

18.2.4. Electronic Signatures within IRBManager

The first sign-in to the system requires a three- part identifier, consisting of username, password and ClientID. Subsequent signings are executed by entering the password.

Each individual user is accountable and responsible for actions initiated under their electronic signature. Each user is accountable and responsible for maintaining confidentiality of their username and password and must not disclose their username and password to anyone else. Each user must contact the IRB Office and Computing Services to report any potential compromise of their password.

An audit trail of all actions, including signing, that occur within the system is maintained by IRBManager.

References: FDA 21CFR11, Guidance for Industry Part 11, Electronic Records; Electronic Signatures- Scope and Application. Issued August 2003, IRBManager and Validation, Revision: 2011-06, PBRC Policy 603.00

19.0 Deception or Incomplete Disclosure in Research Policy

19.1 Overview

Some research, particularly psychology and behavioral, deliberately withholds information about the purpose of the research and /or the procedures employed or purposely misleads participants by providing false information about some aspects of the research. This policy describes the special responsibilities imposed on the investigator and the considerations required of the IRB when research involves deception or incomplete disclosure.

19.2 Definition(s)

Deception: occurs when an investigator gives false information to subjects and intentionally misleads them about some key aspect of the research. A key aspect includes but is not limited to a primary endpoint.

Incomplete disclosure: occurs when an investigator withholds information about the specific purpose, nature, or other aspect of the research.

See Section 19.8 for Examples

19.3 When Deception May be Used

The following guidelines from The American Psychological Association (APA) explain when deception is appropriate in research:

- Researchers do not conduct a study involving deception unless they have determined that the use of deceptive techniques is justified by the study's significant prospective scientific, educational, or applied value and that effective non-deceptive alternative procedures are not feasible.
- Researchers do not deceive prospective participants about research that is reasonably expected to cause physical pain or severe emotional distress.
- Researchers explain any deception that is an integral feature of the design and conduct of an experiment to participants as early as is feasible, preferably at the conclusion of their participation, but no later than at the conclusion of the data collection, and permit participants to withdraw their data.

19.4 Elements of Waiver of Informed Consent

In studies involving deception or incomplete disclosure as determined by the IRB, fully informed consent is not obtained from participants prior to participation. When the consent process will not fully inform participants about the research, the IRB must consider whether the research meets all the criteria for a waiver of one or more elements of informed consent as set forth in federal regulations at 45 CFR 46.116(d).

The criteria for a waiver of one or more elements of informed consent are:

- The research involves no more than minimal risk to participants.
- The waiver or alteration will not adversely affect the rights and welfare of participants.
- The research could not practicably be carried out without the waiver or alteration.
- Whenever appropriate, the participants will be provided with additional pertinent information after participation.

A waiver or alteration of informed consent request must be included in the application to the IRB if deception or incomplete disclosure in research is used in a study.

19.5 Goals of Debriefing

When a researcher uses deception, a debriefing at the end of the study is required, when appropriate. Debriefing may be inappropriate if debriefing regarding the deception may cause more harm than the deception itself.

Debriefing after deception has several goals: (1) to repair the breach of informed consent entailed by the deception, (2) to remove any confusions or defuse any tensions that might have been generated by the deception, (3) to make it clear especially to younger participants that deception is permissible only in exceptional circumstances, and (4) to repair (as much as possible) the breach of trust that has occurred not only between the investigator and the participant, but (potentially) between all researchers and all participants.

19.5.1 Debriefing Guidelines

Ethical Principles of Psychologists and Code of Conduct guidelines discuss debriefing participants of the deception used in research.

- Researchers provide a prompt opportunity for participants to obtain appropriate information about the nature, results, and conclusions of the research, and they take reasonable steps to correct any misconceptions that participants may have of which the psychologists are aware.

- If scientific or humane values justify delaying or withholding this information, researchers take reasonable measures to reduce the risk of harm.
- When researchers become aware that research procedures have harmed a participant, they take reasonable steps to minimize the harm.

19.6 Investigator Responsibilities

The application and protocol submitted to the IRB must include the following:

- Justify the reason for deceiving or withholding information from the participants. This includes an explanation of the research's benefits and why the deception or incomplete disclosure is necessary.
- Explain why the deception or incomplete disclosure is necessary.
- Outline the process of debriefing, if applicable; including when, how and by whom the information will be provided to participants.
- Provide a copy of your debriefing script, if available/applicable.

19.7 IRB Considerations

The IRB must consider the following when reviewing research with deception or incomplete disclosure:

- The IRB must determine that the research qualifies for a waiver or alteration of the required elements of informed consent, in accordance with criteria provided in federal regulations at 45 CFR 46.116(d)
- The scientific value and validity of the research
- The efficacy of alternative procedures
- The certainty that deception or incomplete disclosure does not extend to influence participant's willingness to participate.
- The possibility of experimentally induced harm and the ability of the proposed procedures to remove such harm through debriefing.
- The potential of the deception or incomplete disclosure to facilitate unwanted and inappropriate invasions of privacy.
- Whether the researcher has the skill and resources to address participants' who become upset
- If the study does not involve a de-briefing, the IRB must consider and document the reasoning of why the risks do not outweigh the benefits in not de-briefing participants.

19.8 Examples of Deception and Incomplete Disclosure in Research

- Participants complete a quiz, and are falsely told that they did very poorly, regardless of their performance.
- Participants (who do not know they are in a research study) are observed to see how they behave when they find a large amount of cash in a public location.
- In a study of anxiety, participants are told to expect mild pain during the study, but no painful procedures are administered.

19.8.2 Incomplete Disclosure Examples

- Participants are asked to complete a quiz for research, but not told that the research question involves how background noise affects their performance.
- Subjects are told they are completing study questionnaires to evaluate their satisfaction when the true purpose of the study is to correlate psychiatric symptoms with subject satisfaction.

20.0 Internet Based Research

20.1 Purpose

The purpose of this document is to provide guidance to Pennington Biomedical research investigators, research staff and IRB members concerning responsibilities and considerations related to Internet or mobile technology based human subject research.

20.2 Applicability

This policy applies to the use of the Internet or other technology as a tool for subject recruitment or as a tool for data collection.

20.3 Definitions

Internet Research: The broad and overarching term "Internet research" includes both the Internet as a tool for research and the Internet as a locale or venue for conducting research. For the purposes of this policy, this also includes mobile technology and devices.

Examples of Internet Research[1]

- Study of data already available on the internet without direct interaction with human subjects (harvesting, mining, profiling, scraping—observation or recording of otherwise-existing data sets, chat room interactions, blogs, social media postings, etc.)
- Research that uses the Internet as a vehicle for recruiting or interacting, directly or indirectly, with subjects (Self-testing websites, survey tools, Amazon Mechanical Turk®, etc.)
- Research about the Internet itself and its effects (use patterns or effects of social media, search engines, email, etc.; evolution of privacy issues; information contagion, etc.)
- Research about Internet users—what they do, and how the Internet affects individuals and their behaviors.
- Recruitment in or through Internet locales or tools, for example social media, push technologies

Note: Use of the PBRC web screener by itself does not constitute internet research.

[1] Considerations and Recommendations Concerning Internet Research and Human Subjects Research Regulations, with Revisions, Final document, approved at SACHRP meeting March 12-13, 2013.

Research: systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge. 45 CFR 46.102(b)

Human Subject: a living individual about whom an investigator (whether professional or student) conducting research obtains (1) Data through intervention or interaction with the individual, or (2) Identifiable private information. DHHS 45 CFR 46.102(f) (1&2)

Private Information: includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record). Private information must be individually identifiable (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information) for obtaining the information to constitute research involving human subjects. DHHS 45 CFR 46.102 Definitions

If individuals intentionally post or otherwise provide information on the Internet, such information should be considered public unless existing law and the privacy policies and/or terms of service of the entity/entities receiving or hosting the information indicate that the information should be considered —private. This determination is subject to IRB approval.

Intervention: includes both physical procedures by which data are gathered and manipulations of the subject or the subject's environment that are performed for research purposes. DHHS 45 CFR 46.102 Definitions

Examples of *Intervention*; Mimicking “real-world” manipulations through avatars, Responses to web queries, recording internet-based activities or behaviors for subsequent analysis, Using the internet as a reminder or interface for the performance of some physical activity (e.g., reminder to take medicine or perform a task).[2]

Interaction: includes communication or interpersonal contact between investigator and subject. DHHS 45 CFR 46.102 Definitions

Examples of *Interaction*; Virtual worlds, Guilds to social media sites to chat rooms, Newsgroups, Mobile platforms, Interviews, Focus Groups

[2] Considerations and Recommendations Concerning Internet Research and Human Subjects Research Regulations, with Revisions, Final document, approved at SACHRP meeting March 12-13, 2013.

Individually Identifiable: Identifiable private information is private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information. (Definitions: Federal Register.45 CFR 46)

Private Information: includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (Definitions: Federal Register.45 CFR 46)

Social Media: includes online and mobile resource that provides a forum for generating, sharing, or discussing ideas and content. Specific applications and web tools are variably grouped as online communities (e.g., patient support groups, population-specific dating services); social networking (e.g., Facebook; Twitter); professional networking (e.g., LinkedIn); content production and sharing (e.g., YouTube, Tumblr, blogs); location-based services (e.g., Google Maps); and others.

20.4 Regulatory Review of Internet Research

20.4.1 Policy

Any internet research conducted by an investigator that obtains data through an intervention or interaction with the individual or obtains identifiable private information must be reviewed by the IRB. Some research may be exempt from IRB oversight; however, the IRB will exempt research based upon categories allowed as per 45 CFR 46.101. Exemption Categories can be found in Policy 3.

20.5 IRB Considerations

20.5.1 Privacy and Confidentiality Considerations

IRBs must ensure that adequate provisions are in place to maintain confidentiality of research data and privacy of research subjects.

IRBs will consider:

- The implications of the researcher and the public's ability to re-identify subjects; and
- Provisions for accurately informing subjects of mechanisms in place for ensuring confidentiality of research data as opposed to ensuring anonymity.

20.5.2 Informed Consent Considerations

- When appropriate, the IRB may grant a waiver of informed consent or waiver of documentation of the informed consent as per HRPP Policy 5, Obtaining Informed Consent from Research Subjects and DHHS 45 CFR 46.116.
- For research that meets the criteria for a waiver of documented informed consent, the internet site should provide potential subjects with information about the research, and a button to click to agree to participate. The contents of the information site must receive Pennington Biomedical IRB review and approval prior to implementation.

20.6 Investigator Responsibilities

Investigators should be familiar with the terms of service and privacy policy for each Internet research technology to be used in their research prior to the research being approved.

20.6.1 Protocol Considerations

- Providing the IRB with the investigator's assessment of how subject's privacy and confidentiality will be protected using the Internet research.
- Providing the IRB with the safeguards the investigators will use to protect subjects from an invasion of privacy or breach of confidentiality.
- Providing the IRB with a plan on how subjects will be informed of their risks of invasion of privacy and breach of confidentiality associated with the specific use of Internet research.

20.6.2 Informed Consent Considerations

- Investigators should include all the required elements of informed consent as stated in the federal regulations when generating consent documents for online research. When online research is being employed, the PBRC online consent form template should be followed, unless a waiver or alteration of informed consent is granted by the IRB.

20.6.2 Email Address for Investigators

Pennington Biomedical investigators are required to use their Pennington email address or a Pennington Biomedical departmental email address for communications

related to research in which Pennington Biomedical consider the institution engaged in research. Investigators should register with their Pennington email address when registering with on-line services, databases and cloud services for research-related purposes.

20.7 Research with Minors in Internet Research[3]

- PBRC does not allow internet research to be conducted in children under the age 13 to comply with Children's Online Privacy Protection Act (COPPA) regulations.
- The protocol needs to describe methods to verify age of minor.

20.8 Data Security and Data Collection

- It is strongly recommended that any data collected from subjects over computer networks be transmitted in encrypted format. This helps ensure that any data intercepted during transmission cannot be decoded and that individual responses cannot be traced back to an individual respondent.
- It is recommended that the reasonable and appropriate be used as determined by the IRB. This may require that the study participants be encouraged or required to use a specific type or version of browser software.
- Researchers are cautioned that encryption standards vary from country to country and that there are legal restrictions regarding the export of certain encryption software outside US boundaries.

20.9 Recruiting Through the Internet

Subject recruitment using the internet must follow the IRB guidelines for advertisements that apply to any traditional media, such as newspapers and bulletin boards. (See Advertisements section in Policy 3 for further information.) [4]

- Investigators should check that their proposed recruitment strategies comply with the policies and terms of use of the sites they wish to use and should provide documentation of HIPAA compliance with the assistance of Legal and Regulatory Compliance before submission to the IRB.

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[3] COPPA – Title XIII, Sec. 1302 (1) child means "age 13" and Title XIII, Sec. 1303 (a) (1) (ii)

[4] The available federal guidance: (1) OHRP, Guidance on Institutional Review Board Review of Clinical Trial Websites (http://www.hhs.gov/ohrp/policy/clinicaltrials.html); (2) SACHRP, Considerations and Recommendations Concerning Internet Research and Human Subjects Research Regulations (http://www.hhs.gov/ohrp/sachrp/mtgings/2013%20March%20Mtg/internet_research.pdf); and (3) FDA Information Sheet, Recruiting Study Subjects: Guidance for Institutional Review Boards and Clinical Investigators (http://www.fda.gov/RegulatoryInformation/Guidances/ucm126428.htm)

20.10 Miscellaneous

20.10.1 Characteristics of Purely Public Sites

- Sites containing information that, by law, is considered —public.
- News, entertainment, classified, and other information-based sites where information is posted for the purpose of sharing with the public.
- Open access data repositories, where information has been legally obtained (with IRB approval if necessary) and is made available with minimal or no restriction.
- Discussion fora that are freely accessible to any individual with Internet access, and do not involve terms of access or terms of service that would restrict research use of the information.

20.11 HIPAA

20.11.1 Definitions

PHI - Protected Health Information: for purposes of this policy means individually identifiable health information that relates to the past, present or future research services provided to an individual.

Authorization: a written document completed and signed by the individual that allows use and disclosure of PHI for purposes other than treatment, payment or health care operations.

20.11.2 HIPAA Policy

Any protected health information (PHI) collected is subject to the Pennington Biomedical HIPAA policies and requires a HIPAA authorization. The following identifiers which constitute PHI:

20.11.2.1 Protected Health Information Identifiers

a. Names (this includes initials)
b. All geographic subdivisions smaller than a state including street address, city, county, precinct, ZIP Code, and their equivalent geographical codes, except for the initial 3 digits of a ZIP Code if according to the current publicly available data from the Bureau of the Census:
c. The geographic unit formed by combining all zip codes with the same three initial digits contains more than 20,000 people AND

d. The initial three digits of a zip code for all such geographic units containing 20,000 or fewer people is changed to 000.
e. All elements of dates (except year) for dates directly related to an individual, including birth date, admission date, discharge data, date of death, and all ages and elements may be aggregated into a single category of age 90 or older.
f. Telephone numbers
g. Fax numbers
h. Electronic mail addresses
i. Social Security numbers
j. Medical Record numbers
k. Health plan beneficiary numbers
l. Account numbers
m. Certificate/license numbers
n. Vehicle identifiers and serial numbers, including license plate numbers.
o. Device identifiers and serial numbers
p. Web Universal Resource Locators (URLs)
q. Internet Protocol (IP) address numbers
    1. Biometric identifiers, including finger and voice prints.
    2. Full face photographic images and any comparable images
r. Any other unique identifying number, characteristic or code, except as permitted by 45 CFR 164.514(c).[5]

20.11.3 De-Identification

PHI may be de-identified by removing all the identifiers listed above. Once the identifiers are removed, the information is no longer subject to HIPAA protection.

20.11.4 Waiver of HIPAA Authorization.

20.11.4.1 PBRC may use or disclose PHI for research if it obtains IRB approval of an alteration to or waiver, in whole or in part, of the individual's authorization required for use or disclosure of PHI.

20.11.4.1.1 Waiver Criteria

A statement that the IRB and/or Privacy Board have determined that the alteration or waiver, in whole or in part, of authorization satisfies the following criteria:

[5] Guidance Regarding Methods for De-identification of Protected Health Information in Accordance with the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule, U.S. Department of Health and Human Services

a) The use or disclosure of PHI involves no more than minimal risk to the individuals based on, at least, the presence of the following elements:
    i. There is an adequate plan to protect the identifiers from improper use and disclosure.
    ii. There is an adequate plan to destroy the identifiers at the earliest opportunity consistent with conduct of the research, unless there is a health or research justification for retaining the identifiers, or such retention is otherwise required by law.
    iii. There are adequate written assurances that the PHI will not be reused or disclosed to any other person or entity, except as required by law, for authorized oversight of the research study, or for other research for which the use or disclosure of PHI is permitted.
b) The research could not practicably be conducted without the alteration or waiver; and
c) The research could not practicably be conducted without access to and use of the PHI.

20.11.4.1.2 PHI Needed

A brief description of the PHI for which use, or access has been determined to be necessary and without which the research could not practicably be conducted as determined by the IRB and/or Privacy Board.

20.11.5 Notice of Privacy Practices

As per Pennington Biomedical policies the Notice of Privacy Practices should be available for subjects to print when conducting internet surveys.

21.0 Collaborative Research

21.1 Policy

In the conduct of collaborative or cooperative research projects, each institution (or entity) is responsible for safeguarding the rights and welfare of human subjects and for complying with any applicable regulations. Federal regulations allow for cooperative research projects which involve more than one institution. To avoid duplication of review efforts by IRBs, this institution may choose to conduct joint reviews, rely upon the review of another qualified IRB, provide review oversight for another IRB, or make other arrangements to establish an alternate oversight plan.

For nonexempt research involving human subjects, the institution shall document the reliance of the IRB for oversight of the research and the responsibilities that each entity will undertake to ensure compliance with the requirements in a written agreement or as set forth in a research protocol. Exempt research that involves limited IRB review under 45CFR46.104(d)(2)(iii), (d)(3)(i) (C), (d)(7), or (d)(8) of the revised common rule requires a reliance agreement whenever the reviewing IRB (aka the IRB of record) is not operated by the institution.

This institution may rely upon the review of another qualified IRB if the institution has a current, unexpired Federalwide Assurance (FWA) on file with the Department of Health and Human Services (DHHS) Office for Human Research Protections and one of the following criteria are met:

- The IRBs are part of an AAHRPP accredited institution.
- This institution's investigator is a collaborator on Human Research that is primarily conducted at another institution and the investigator's role does not include interaction or intervention with subjects.
- The institution is engaged in the Human Research solely because it is receiving federal funds, even where all activities involving human subjects are carried out by employees or agents of another institution. (Employees and agents of this institution do not interact or intervene with subjects, gather, or possess private identifiable information about subjects, nor obtain the consent of subjects.)
- When this institution is engaged in the research and the greatest level of risk to study subjects occurs at another institution, this institution may agree to rely on that site's IRB. This policy assumes the IRB at the non-PBRC site will have the required reviewer expertise. If it does not, the IRB with the required reviewer expertise will be selected from among engaged Institutions.
- Mandated by NIH Single IRB Policy for Multi-site Research.

The OHRP Guidance on Engagement of Institutions in Human Subjects Research will be used as the basis for determining engagement in human-subjects research. Such determinations will be made in collaboration and consultation with authorized representatives at this institution and the collaborating institution and/or the collaborating individual investigators, whichever is most appropriate.

Regulations & Guidance: HRPP Policy 302, FDA 21 CFR 56.114, DHHS 45 CFR 46.103(e) ,114, and NIH NOT-OD-16-094

21.2 Definitions

Agreement: may be referred to as a Cooperative Agreement, IRB Authorization Agreement (IAA) or IRB Reliance Agreement. When the agreement is designed to cover all future multi-site studies involving two or more sites, this is usually referred to as a Master Reliance Agreement.

Cede review: the act of transferring IRB review and oversight.

Collaborating institutional investigator: not otherwise an employee or agent of the assured institution; conducting collaborative research activities outside the facilities of the assured institution; and is acting as an employee or agent of an institution that does not hold an OHRP-approved FWA with respect to his or her involvement in the research being conducted by the assured institution; and employed by, or acting as an agent of, an institution that does not hold an OHRP-approved FWA and does not routinely conduct human subjects research.

Collaborative (also-known-as Cooperative or Multi-site) research: studies involving more than one institution.

Federalwide Assurance (FWA): a contract or agreement that establishes standards for human subjects research as approved by the Office for Human Research Protections (OHRP).

IRB of Record (also known as the Lead, Reviewing or Central IRB): means the IRB who is responsible for the review, approval, and regulatory oversight of a multi-site research study.

Individual Investigator Agreement (IIA): An IIA is an agreement between PBRC and an individual collaborator who is not affiliated with an FWA institution (e.g., former student working after graduation with their faculty mentor, professional in the community with specific expertise, community partners). This agreement type outlines the

responsibilities of the individual investigator for the protection of human subjects. The IIA is signed by all the following:

- Individual investigator
- PBRC Principal Investigator (PI)
- PBRC Institutional Official or designee

IRB Authorization Agreement (IAA): An IAA is an agreement between PBRC and another institution that holds a Federal Wide Assurance (FWA) with the Office of Human Research Protections (OHRP) of the U.S. Department of Health and Human Services (HHS). Any institution (e.g., university, medical centers, NGOs, community organization, survey research organization) receiving funds from HHS must have an FWA. This agreement type is used to establish the IRB-of-Record (whether that's PBRC or the other institution). The IAA is signed by the Institutional Officials or designee at each institution.

Lead PI: The principal investigator with ultimate responsibility for the overall conduct, safety, regulatory oversight, and data integrity for a multi-site research study.

Local Context Language: language specific to the conduct of human subjects research at each institution (e.g., subject injury language, HIPAA authorizations, data security, unique state or local laws, local practices or cultural issues, etc.).

Master Reliance Agreement (MRA): A MRA can be utilized when multiple studies are ceding review to a specific external IRB. Master Agreements may be reciprocal in that signatory institutions can act as the site providing IRB review and oversight or the site relying. Master Reliance Agreements may be for a single protocol or a number of protocols and are negotiated on a case by case basis. MRA eliminates the need for separate IAAs and individual negotiation and documentation. The PBRC IRB currently has master agreements in place with the following external reliance platforms:

- IRB Reliance Exchange (IREx)
- Smart IRB

Multi-site Review: Where one IRB accepts responsibility to serve as the IRB of record.

Multi-site study: a study where the same protocol is to conduct non-exempt human subject research at more than one site.

Participating Institution: a domestic entity that is a signatory party to the Reliance Agreement. The institution will rely on the lead IRB to carry out the site’s IRB review of human subjects research for the multi-site study.

Relying Institution or Site: A hospital, clinic, doctor's office where research will take place, and which will rely on an external IRB (Central IRB) which will serve as the

Reviewing IRB for a multi-site study. When academic institutions are involved, this term incorporates the Relying IRB and the Relying Participating Institution

Relying Site Investigator: A Principal Investigator at the Relying Institution for a study that may be overseen by a Lead or an external IRB.

"Same research protocol": a protocol that addresses the same research questions, involves the same methodologies, and evaluates the same outcomes are considered to be the "same research protocol." Additionally, sites that are accruing research participants for studies that are identical except for variations due to local context consideration would be conducting the "same research protocol."

Site PI: A principal investigator who is responsible for the conduct of the research at their Participating Institution.

21.3 IRB Authority

This institution must approve research conducted by its employees or agents, regardless of the location of the study before the research can begin. Thus, even in cases when a research project is performed at another institution, employees must contact the PBRC IRB to determine the level of engagement in human subjects research. This standard holds even if researcher's participation is as co-investigator, or the researcher has a limited role.

IRB approval at this institution does not extend to individuals on the project who are affiliated with other institutions. Those individuals must seek IRB review from their IRB of record, obtain an individual investigator agreement, or cede review through a reliance system.

The Executive Director of Pennington Biomedical Research Center is designated as the Institutional Official. The Institutional Official (IO) is vested with the authority to execute IRB reliance agreements on behalf of this institution. The IO may delegate this authority.

Legal Counsel facilitates arrangements of Single IRB review mechanisms as needed through an approved Reliance Agreement or Memorandum of Understanding (MOU). Initial review and subsequent reviews are conducted by the IRB of record for that study and in accordance with the arranged agreement between entities.

The IRB Chair and other individual(s) with sufficient expertise and authority may review investigator requests and determine the appropriateness of reliance on a case-by-case basis. However, all applicable parties (e.g., legal, conflict of interest review, clinical staff, pharmacy, radiation safety, biosafety review, license and technology, sponsored project

services, etc.) are consulted regarding the reliance. If applicable, investigators must submit all additional required reviews to the IRB. Studies approved through reliance agreements are communicated to the IRB board in the meeting minutes.

The HRPP Director or designee will facilitate communication with the relying or reviewing institution about IRB actions on the human subjects research that is subject to the agreement, in accordance with its specific provisions.

21.4 NIH Single IRB Policy for Multi-Site Research

The National Institutes of Health (NIH) Policy on the Use of a Single Institutional Review Board for Multi-Site Research is effective for NIH grants submitted on or after January 25, 2018. The policy applies to NIH-funded multi-site studies where each site will conduct the same protocol involving non-exempt human subject research and requires that a single IRB (single IRB) provide IRB approval for all participating sites.

If all the conditions below are met, the NIH Single IRB Policy is applicable:

- The policy applies to domestic awardees and participating domestic sites only; foreign sites participating in NIH-funded, multi-site studies are not expected to follow this policy.
- The policy applies to Research Grants (R or U series) or a Program Project/Center Grant (P series).
- The human subject research is not exempt. The research requires IRB review and approval at the Expedited or Full Board level.
- Two or more U.S. sites/institutions conduct the research.
- The same protocol will be conducted at each U.S. site/institution:
    - Protocols that address the same research questions, involve the same methodologies, and evaluate the same outcomes and the only variations are in enrollment of subjects due to local context considerations; or
    - A separate site is used for study coordination or coordination of data and statistical analysis.
- Exceptions to the policy can be requested, based on law or regulation, or due to some other compelling reason.

The NIH Single IRB Policy does not apply to:

- Career development (K), research training (T) or fellowship awards (F) awards.
- Ongoing projects that are not being submitted for consideration of a competing grant (such as noncompeting continuing grant).
- Other Transaction Agreements (OTAs) under the authority of the Department of the Defense (DoD).

- Foreign research collaborating institutions/sites.
- Projects awarded before NIH sIRB effective date.

In some cases, NIH (or another funding sponsor) may specify the single IRB in the Funding Opportunity Announcement (FOA) or a request for proposal (RFP) funding announcement. However, for most grants, NIH expects the lead PI to identify a specific single IRB in the grant application.

Absent an NIH mandate to rely on a single IRB, the PBRC IRB will consider the risks to participants as well as the capacity and expertise for serving as the IRB of record for the study or ceding review to another institution. Exceptions for other federally funded research may be requested through the IRB Office and will be considered on a case-by-case basis.

21.5 Requirements for Single IRB Review under the Revised Common Rule

The Revised Common Rule extends the Single IRB review requirement to all "cooperative research."

- Required compliance effective date for this provision: January 20, 2020.

All research funded by any federal agency that is a signatory to the Common Rule must comply.

21.6 OHRP Exception to Single IRB Review

OHRP determined that for HHS cooperative research subject to the revised Common Rule (also referred to as the 2018 Requirements), and for purposes of 45 CFR 46.114(b)(2)(ii), an institution may continue to use multiple IRBs, in lieu of a single IRB, for the following research:

1. Cooperative research conducted or supported by HHS agencies other than the National Institutes of Health (NIH), if an IRB initially approved the research before January 20, 2020.

2. Cooperative research conducted or supported by NIH if either:

    a. the NIH single IRB policy does not apply, and the research was initially approved by an IRB before January 20, 2020.

    b. NIH exempted the research from its single IRB policy before January 20, 2020.

According to OHRP any institution located in the United States that is engaged in cooperative research must rely upon approval by a single IRB for that portion of the

research that is conducted in the United States. The reviewing IRB will be identified by the Federal department or agency supporting or conducting the research or proposed by the lead institution subject to the acceptance of the Federal department or agency supporting the research. In certain circumstances, the single IRB does not apply (reasons of law or as determined by the federal department or agency conducting or supporting the research). For example, cooperative research for which more than single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe); or Research for which any Federal department of agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate.

Regulations [§46.114(b)(1): (b)(1)]

21.7 Reliance Agreements

Reliance agreements (or authorization agreement) between institutions is established through a legal agreement and may apply to the review of one study, to certain specific categories of studies or to all studies. This means that the PBRC IRB may become the IRB of Record (lead or reviewing IRB) or cede oversight of the research activity to another equally qualified IRB and become the relying IRB. Under the arrangement, IRBs may compare best practices, share SOPs and informed consent documents, and pool resources to facilitate a review.

A reliance agreement can be in many different forms, but some of the main agreements are Institutional Authorization Agreements (IAA), and Master Reliance Agreement (MRA). Such agreements are limited to IRB review, and do not include identification and management of researcher conflicts of interest and review by ancillary committees such as radiation safety and biosafety and are unnecessary for research that qualifies as “exempt” under 45 CFR 46.101(b).

When following the NIH policy, the reliance agreement must document respective authorities, roles, responsibilities, and communication between an organization providing the ethical review and a participating organization relying on a reviewing IRB.

A reliance agreement is applicable and necessary only when both institutions are "engaged" in human subjects research. For example, if one site is only analyzing coded, de-identified data, and no one at that site can ever access the key linking codes to identifiers, then that site may not be "engaged" in human subjects research.

21.8 Selection of the IRB of Record

There is a minimum set of requirements to assist in the selection of the IRB of record. The evaluation criteria include the following:

- Evidence of a commitment to the highest ethical standards and ability to meet rigorous standards for quality and protection of research participants, e.g., through accreditation or assessment of policies, procedures, and practices.
- Ability to meet regulatory requirements.
- Well-established track record of compliance and performing high quality reviews, e.g., no regulatory errors or failures with Department of Health and Human Services (DHHS) or Food and Drug Administration (FDA).
- Appropriate expertise and experience to review the proposed research and the capacity to review the study protocol and participating site study documents.
- Recognition of the importance of building trust across all sites.
- Capacity to develop and maintain the respect and trust of the research participants and the communities in which the research is performed.
- Willingness and ability to serve as a Privacy Board to fulfill the requirements of the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule for use or disclosure of protected health information for research.
- Adherence to communication standards and a commitment to transparency through sharing information about the review process, e.g., meeting minutes, approval status.
- Adequate institutional infrastructure and support, and evidence of quality and robustness of the institution's human research protection program.
- Sufficient staff to handle communications between all sites for initial review, continuing review, adverse events, amendments, etc.
- Available interoperable information technology resources to facilitate communication and exchange of information between the participating institutions.
- Sufficient resources to negotiate and track authorization agreements.
- Ability to account for the IRB costs for review and management and how those costs will be met.
- Adequate processes in place and administrative support to handle additional review responsibilities; and
- Institutional impact the single IRB (sIRB) will have on the institution's HRPP policies, accreditation status, tracking and management processes.

21.9 Responsibilities when PBRC is the Lead Site or Reviewing IRB

21.9.1 Organization

1. Ensuring that the composition of the IRB is appropriate for the research to be reviewed and complies with applicable laws.
2. Ensuring that business functions are separated from IRB review.

3. Conducting IRB review of research according to all applicable regulations and laws, including initial review, continuing review, and review of modifications.
4. Conducting review of the addition of investigative sites to previously approved protocols. The IRB may decide to review these additions as separate protocols or as modifications to previously approved research, and they may decide to handle such modifications using the expedited procedure rather than the convened IRB for review. When the expedited procedure is used, the IRB must specify the criteria for when the addition of an investigative site is a minor modification.
5. Ensuring that the organization has final authority to determine whether researcher/staff conflict of interest and any proposed management allows the research to be approved.
6. Reviewing unanticipated problems involving risks to subjects or other.
7. Ensuring procedure for suspending or terminating approval.
8. Having procedures for notifying the researcher of IRB decisions and, if applicable, the relying organization.
9. Making available relevant IRB records, including but not limited to minutes, approved protocols, consent documents, and other records that document the IRB's determinations to the relying organization upon request.
10. Having the authority to perform or request an audit of research under its review.
11. Making relevant IRB policies readily available to the relying organization and communicating updates to the relying organization as needed.
12. Specifying the contact person/contact information for the reviewing IRB so researchers/staff can ask questions, express concerns, and convey suggestions.
13. Records must include documentation specifying the responsibilities that a relying organization and an organization operating an IRB each will undertake compliance with the requirements of the Common Rule. (45CFR46.103(e)

21.7.2 Principal Investigator

1. The PBRC investigator must complete the IRB Cede Review Request form to initiate the reliance review process.
2. Ensuring that any necessary internal organizational reviews and approvals are obtained.
3. Assisting the PBRC IRB in obtaining information about the external site's local requirements or context relevant to the research.
4. Submitting all relevant documents to the IRB (e.g., protocol, consent forms, modifications to previously approved research, continuing reviews, etc.).

5. Ensuring reporting of any proposed changes to the research to the PBRC IRB prior to implementation unless the change is necessary to eliminate apparent immediate hazards to the subject(s).
6. Ensuring reporting of any unanticipated problems involving risks or others in accordance with the reliance agreement.
7. Ensuring researchers provide data safety monitoring to the PBRC IRB.
8. Ensuring reporting of noncompliance, complaints, deviations, and other reports in accordance with the PBRC reporting requirements.
9. Ensuring adequate space and resources are available to conduct the study.

21.10 Responsibilities when PBRC is the Relying Organization (when PBRC is NOT the IRB of Record)

21.10.1 Organization

The organization must ensure that the lead organization's policies and procedures describe the roles of the organization and researchers when relying upon another organization's IRB, including:

1. Specifying the internal contact person so researchers and staff may ask questions, express concerns, and convey suggestions regarding the use of the reviewing IRB.
2. Ensuring through education or other support, that researchers understand which activities are eligible for review by another IRB.
3. Ensuring that researchers/staff have the appropriate education/training, qualifications, expertise, and knowledge to conduct the research and fulfill their responsibilities and obligations under law, regulation, guidance, or policy.
4. Complying with the determinations and requirements of the reviewing IRB.
5. Providing the reviewing IRB with requested information about local requirements or local research context issues relevant to the IRB's determination, prior to IRB review.
6. Notifying the reviewing IRB when local policies that impact IRB review are updated.
7. Ensuring that researchers of the relying organization may not approve research subject to the reliance agreement if it has not been approved by the reviewing IRB.
8. Acknowledging that researchers must cooperate in the reviewing IRB's responsibility for initial and continuing review, record keeping, and reporting, and that all information requested by the reviewing IRB must be provided in a timely manner.

9. Requiring researchers and research staff disclose conflicts of interest according to the process agreed upon between the organization and reviewing IRB and comply with any conflict-of-interest management plans that may result.
10. Reporting promptly to the reviewing IRB any proposed changes to the research. The investigator cannot implement changes to the research (including changes in the consent document) without prior IRB review and approval, except where necessary to eliminate apparent immediate hazards to the participants.
11. Ensuring researchers will not enroll participants in research prior to review and approval by the reviewing IRB and meeting all other applicable requirements and approvals for the study.
12. Ensuring that researchers, when responsible for enrolling participants, will obtain, document, and maintain records of consent for each participant or each participant's legally authorized representative.
13. Reporting promptly to the reviewing IRB any unanticipated problems involving risks to participants or others according to the requirements specified in the reliance agreement.
14. Ensuring researchers provide to the reviewing IRB data safety monitoring reports they receive, according to the IRB's reporting policy.
15. Ensuring reporting of non-compliance, participant complaints, protocol deviations or other events according to the requirements specified in the reliance agreement.
16. Conducting monitoring in addition to, or in cooperation with, the reviewing IRB, when appropriate.
17. Specifying the contact person and providing contact information for researchers and research staff to obtain answers to questions, express concerns, and convey suggestions regarding the use of the reviewing IRB.
18. Ensuring researchers and research staff have appropriate qualifications and expertise to conduct the research, are knowledgeable about laws, regulations, codes, and guidance governing their research, and are knowledgeable about the organization's policies and procedures.

21.10.2 Principal Investigator

1. PBRC Investigators submit the following to the IRB when another IRB is serving as the IRB of Record:
    a. All funding information (including a copy of the grant, if available).
    b. Key Study Personnel and their qualifications.
    c. Any basic information about the study type and reviewing IRB.
    d. A description of the study.

e. All enrollment information for participants at PBRC.
f. A description of all drug/devices that will be used during the study, and safety information, if applicable.
g. A description of any PHI to be used/disclosed, if applicable.
h. Any conflicts of interest.
i. The IRB approved consent including local context information and PBRC-specific language (e.g., HIPAA authorization and subject injury language).
j. The IRB approved study protocol.
k. The IRB approval letter from the reviewing IRB.
l. Reports of non-compliance and adverse events/unanticipated problems that occur at PBRC; and
m. Submitting all relevant IRB records, including but not limited to minutes and other records documenting IRB determinations to the relying organization upon request.

21.11 Responsibilities Delegated to Reviewing or Relying Organizations

1. Providing education to researchers and research staff.
2. Conducting scientific review.
3. Ensuring concordance between any applicable grant and the IRB application/protocol.
4. Reviewing requests for waivers of alterations of the requirement for HIPAA authorization, when applicable.
5. Reviewing potential noncompliance, including complaints, protocol deviations, and result audits, including
    - Identifying which organization is responsible for deciding whether an allegation of noncompliance has a basis in fact.
    - Identifying which organization's process is used to decide whether an incident of noncompliance is serious or continuing.
6. Obtaining management plans for researcher and research staff conflicts of interest. If the relying organization maintains responsibility for this issue, the management plan must be provided prior to the decision by the IRB.
7. Managing organizational conflict of interest related to the research.
8. Ensuring that, should termination of a reliance agreement occur, one of the parties is clearly responsible for continued oversight of active research until closure or a mutually agreed upon transfer of the studies.

21.12 When following DHHS or FDA regulations or requirements, the agreement or procedures address:

1. Whether the relying organization applies its FWA to some or all research and ensuring that the IRB review is consistent with the requirements of the relying organization's FWA.
2. Which organization is responsible for obtaining any additional approvals for DHHS when the research involves pregnant women, fetuses, neonates, or children (or any other applicable federal agency or department requirements).
3. Which organization is responsible for reporting serious or continuing non-compliance; unanticipated problems involving risks to participants or others; and suspensions or terminations of IRB or EC approval. Reporting may be done by the reviewing IRB, the relying organization, or jointly, but must be clearly defined in policies or a written agreement.

21.13 When following the NIH Single IRB policy, the agreement or procedures documents or describes:

1. The requirement for single IRB review applies to awardees in the United States and participating research sites in the United States.
2. The requirement for single IRB review does not apply to organizations outside the United States.
3. Awardee organizations are responsible for ensuring authorization agreements are in place, and that documentation is maintained.
4. Who is responsible for meeting additional certification requirements, such as Certificates of Confidentiality or the NIH Genomic Data Sharing Policy.
5. Participating sites are expected to rely on the single IRB, though they may conduct their own review in accordance with NIH policy on exceptions from single IRB review.

21.14 When relying upon an IRB that is not AAHRPP accredited:

1. The HRPP must ensure that the research is being reviewed appropriately and complies with applicable law and regulations.
2. The HRPP will conduct an IRB evaluation review based upon OHRP evaluation tools to confirm compliance with the organization's ethical standards and with applicable law and regulations. The extent of the review of the non-accredited IRB can vary, depending upon the level of risk to participants in the research.

21.15 When additional reviews relevant to the HRPP are conducted by an external organization, the HRPP will:

1. Inform the external review that additional regulatory requirements, for example, those of DoD or DoJ, may apply.
2. Provide education to researchers regarding additional relevant reviews.

22.0 Emergency Preparedness Plan for the Human Research Protection Program (HRPP)

22.1 Scope

This policy establishes written procedures for initiating a response to an emergency/disaster impacting the PBRC Human Research Protection Program (HRPP) or HRPP operations.

This policy outlines emergency planning specific to the Human Research Protection Program (HRPP). It is designed to complement, not replace, the broader emergency response plans established by institutional leadership or institution-wide protocols. HRPP-specific emergency measures apply only to HRPP functions that are not already addressed by the institution's general emergency plans.

22.2 Purpose

The procedures outlined in this policy will be invoked when an emergency/disaster situation impacting the HRPP has occurred, or in preparation for scenarios where a potential emergency situation is imminent (e.g., natural disaster, man-made disaster, infectious disease pandemic, etc.) and HRPP operations and/or the ability of investigators to conduct Human Research is, or is likely to be, adversely impacted.

22.3 Definitions

Emergency or disaster: may include but is not limited to natural disasters, extreme weather events, man-made disasters, and public health crises including infectious disease outbreaks.

22.4 Policy

HRPP leadership defers to the designated institutional authorities and institution-wide disaster and emergency response plans. HRPP-specific planning is limited to operational areas or human research protection activities that are not otherwise addressed by broader institutional plans.

The HRPP director or designee will periodically evaluate the emergency response plans and make changes when appropriate.

The HRPP Director or designee is responsible for carrying out these procedures.

22.5 Procedures

22.5.1 Assess the Nature of the Risk and the Potential Impact to the HRPP

Once an emergency or imminent emergency is identified, determine the response based on the nature of the event. HRPP leadership will contact the appropriate Institutional personnel to determine whether there are Institutional plans already in place to address the event. If these plans are activated, proceed in accordance with those plans and determine whether communication with the research community is necessary to alert them to the activation of the emergency preparedness plan.

22.5.2 Assess Whether the Emergency may Impact HRPP Operations

a. IRB Meetings
   - If the emergency may prevent one or more IRB meetings from occurring, determine whether to cancel or reschedule the meetings, being certain to identify currently approved human research which may expire prior to IRB review. If research will expire, follow IRB Policy 3.12 Continuing Review regarding lapses in continuing review. Because the IRB meets remotely, every attempt will be made to continue IRB meetings to the extent possible.

b. IRB Staff Processing and Member Reviews
   - If staff and IRB chairs will be unable to complete protocol processing and review responsibilities, or if capacity will be limited, IRB leadership will work with the staff to prioritize reviews. If research will expire, follow IRB Policy 3.12 Continuing Review regarding lapses in continuing review.

   - Because the IRB office staff, chair, and reviewers have the capacity to work remotely, every attempt will be made to continue/restore regular IRB office operations as quickly as possible.

22.5.3 Assess Whether the Emergency may Impact Investigators' Ability to Conduct Research

<u>In-person interactions with research subjects:</u> If studies involve in-person interactions with research subjects, organizational leadership will determine whether the studies may be conducted as written while adhering to emergency mitigation strategies.

a. Sponsored Research

   When studies have an external sponsor, ensure coordination with each sponsor to confirm mitigations plans.

b. Clinical Trials Unit

   If the emergency impacts clinical care standards which may in turn impact Research, clarify what does and does not require IRB review. For example, in the case of a public health crisis, screening procedures implemented by the Clinical Trials Unit where a clinical trial is being conducted would not require IRB review/approval of the screening procedures. Conducting research procedures at an alternate clinical care location may require prospective IRB approval. Patient safety will take priority above all other considerations; measures implemented immediately to ensure patient safety may be reported retrospectively. Emergency response plans must be considered for each existing research location.

c. Safety Monitoring

   If trial participants are unable to come to the investigational site for protocol-specified visits, alternative methods for safety assessments must be considered. This may include utilizing phone contact, virtual visits, and/or alternative locations for assessment (including local labs or imaging centers) to assure the safety of trial participants.

22.5.4 Consider Necessary Actions to Address the Impact of the Emergency

The HRPP, in coordination with PBRC leadership and Investigators will determine the actions to take during the emergency to minimize research disruptions. Possible actions include, but may not be limited to, the below.

a. Postponing New Study Implementation

   Consider delaying review and/or startup of new protocols that are non-interventional in nature, present no direct benefit to participants, and do not pertain to the current emergency.

b. Suspending Enrollment/Recruitment on Open Studies

   The institution may need to identify studies for which recruitment and/or enrollment should be suspended, but ongoing study interventions may continue.

c. Continuing Studies via Alternate Mechanisms

   Whenever feasible, adopt online or remote methods for conducting research activities such as recruitment, obtaining consent, data collection, debriefing, and follow-up. Identify additional procedures that can be carried out via telephone, video conferencing, or other digital platforms. If appropriate, consider adjusting the timing of visits and research procedures.

d. Relying on Another Organization to Provide IRB Oversight

Make arrangements (when possible, in advance of an emergency) as necessary to rely upon other organizations for IRB review. Identify the external IRBs and ensure reliance agreements are in place in accordance with IRB Policy 21.0 Collaborative Research.

e. Employing Strategies to Exercise Flexibility in Oversight

For studies not subject to federal regulations, organizations may implement alternative procedures that are equivalent in safeguarding the rights and welfare of research participants. For instance, during emergencies, the IRB may consider extending continuing review timelines for non-federally funded or supported research, and may permit minor protocol changes to be reported at the time of continuing review rather than in advance. Additionally, for most minimal risk studies, regardless of funding source, the IRB may more broadly apply waivers of documentation of consent, particularly when notifying participants of updates to consent forms.

22.5.5 Triage the Research that will be Subject to the Emergency Mitigation Strategies

The organization will consider the types of research that may continue and the types of research that may need to be temporarily postponed. This consideration may include:

a. Studies which present a likelihood of direct benefit to participants (or conversely, studies which include study interventions which may be harmful to subjects if discontinued) should not be postponed, to the extent possible.

b. Research involving direct interactions or interventions may continue if those activities can be conducted through alternative methods, such as remote visits.

c. Studies which may have an adverse impact on resources required to address the emergency must be postponed, if possible.

22.5.6 Develop Education, Training, and Communications on Expectations During an Emergency

Targeted communications and education/training will be developed and distributed based on roles/responsibilities within the HRPP. In particular, researchers and research staff, IRB Chairs and IRB members, IRB Staff, and departmental administrators may each have differing needs regarding effectively responding to emergency mitigation strategies.

PBRC will communicate research-related measures implemented in the event of an emergency via standard communication routes, such as email and web-based platforms, if available. If the standard routes are not available, consult the institutional plans in place to address communications. Ensure the communications include instructions and expectations for impacted personnel.